FOREWORD INTRODUCTION

2-DIMETHYLAMINOETHYL ACRYLATE

CAS N°: 2439-35-2

SIDS Initial Assessment Report

For

SIAM 16

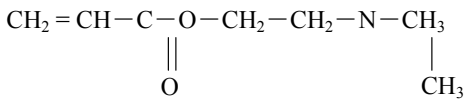
May 27-30, 2003, Paris, France

1.	**Chemical Name:**	2-dimethylaminoethyl acrylate
2.	**CAS Number:**	2439-35-2
3.	**Sponsor Country:**	Japan
		Mr. Yasuhisa Kawamura Director Second International Organisations Div. Ministry of Foreign Affairs 2-2-1 Kasumigaseki, Chiyoda-ku Tokyo 100
4.	**Shared Partnership with:**	Mr. Yuji Ito Nippon Shokubai Co., Ltd. E-mail: hkn@n.shokubai.co.jp
5.	**Roles/Responsibilities of the Partners:**	Atofina, Ciba Specialty Chemicals Inc., Kohjin Co., Ltd., Nippon Shokubai Co., Ltd., Osaka Organic Chemical Industry, Ltd., SNF S.A., Toagosei Co., Ltd.
•	Name of industry sponsor /consortium	
•	Process used	
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme ?	This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 16.
7.	**Review Process Prior to the SIAM:**	Japanese government peer-reviewed the documents and audited selected studies.
8.	**Quality check process:**	Japanese government peer-review committee performed spot checks on randomly selected endpoints and compared original studies with data in the SIDS Dossier.
9.	**Date of Submission:**	July 30, 2003

10. Date of last Update:

11. Comments: None

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2439-35-2
Chemical Name	2-Dimethylaminoethyl acrylate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There is no metabolism data specific to 2-dimethylaminoethyl acrylate. However, based on the fact that the structurally related compound 2-dimethylaminoethyl methacrylate hydrolyzes in simulated saliva and simulated intestinal fluid to methacrylic acid and dimethylaminoethanol, it can be assumed that this substance hydrolyzes to acrylic acid and dimethylaminoethanol in the same circumstances. This is supported by the comparison of acute toxicities between acrylic acid with methacrylic acid and this substance with 2-dimethylaminoethyl methacrylate.

The acute oral LD50, dermal LD50, and inhalation LC50 in rats are 455 mg/kg, 419 mg/kg, and 0.066 mg/L, respectively, therefore this substance is considered to be toxic by inhalation, and slightly toxic by oral and dermal route.

This substance is considered to be severely irritating or corrosive to skin, eye and respiratory tract, and does have a sensitizing potential in animal studies.

A repeated dose 90-day oral toxicity study in rodents [OECD TG 408] was conducted with SD (Crl: CD) rats at 0, 2, 10 and 50 mg/kg/day administered by gavage. At 50 mg/kg/day, the macroscopic lesions were limited to sporadic lung damage that was caused by reflux of stomach content. Judging from the hyperplasia/keratosis or other irritation changes found in forestomach, the reflux is a result of incontinence in the gastro-intestinal tract. This substance was not toxic at 2 and 10 mg/kg/day. At the latter dose-level, treatment-related lesions were found in the forestomach of 4 males, however, these findings were almost of minimal grade which were not regarded to be adverse effects. A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] was also available with SD (Crj: CD) rats at doses of 0, 4, 20 and 100 mg/kg/day administered by gavage. The toxicity revealed is common in the two studies. At 100 mg/kg/day, similar changes compared to those seen at 50 mg/kg/day in the former study was observed. At 20 mg/kg/day, similar changes in the forestomach were observed in 2 males. However, these changes were not statistically significant, and considered to be not toxicologic by the authors. This substance was not toxic at 20 mg/kg/day in both sexes in the combined study. Nevertheless, the NOAEL was considered to be 10 mg/kg/day in the 90-day study, by the author.

This substance did not induce gene mutations in 3 strains of *Salmonella typhimurium* and in *Escherichia coli* but did induce gene mutations in the TA98 strain with metabolic activation in one out of two studies. *In vitro*, this substance was only weakly positive in the highest dose tested in CHL lung cells and human lymphocytes with and without metabolic activation. However, *in vivo*, this substance was negative when administered i.p. at the MTD in a single dose study. Based on the present results, and taking into account data on structurally related substances, it is unlikely that this substance is mutagenic *in vivo*.

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] (0, 4, 20, 100 mg/kg/day) was conducted with SD (Crj: CD) rats. There was no sign of reproductive or developmental toxicity up to 100 mg/kg/day, but maternal toxicity was overt and included death. Furthermore, a teratogenicity study [OECD TG 414] (0, 10, 30, 100 mg/kg/day) were conducted with SD (Crl: CD) rats. At 100 mg/kg/day, 27/299 fetuses showed anomalies (dwarf, adactyly) in external examination and 2/144 fetuses showed anomalies (cleft palate, hydrocephaly, testicular ectopia) in internal examination. The absence of ossification of

various bones (vertebrae, sternebrae) was found in many individuals. Maternal toxicity including death was evident. At 30 mg/kg/day, no teratogenic effects were observed, two females, however, died and this substance was found to be maternally toxic. Fetuses with reduced ossification were found at this dose. At 10 mg/kg, no adverse effect was evident. In the teratology study, the NOAEL for maternal toxicity in rats was 10 mg/kg. Prenatal developmental toxicity was only observed at doses (100 mg/kg) which produced signs of maternal toxicity and mortality. The NOAEL for reproduction/developmental toxicity and teratogenicity are considered to be 10 and 30 mg/kg/day respectively.

Environment

Abiotically 2-dimethylaminoethyl acrylate is hydrolyzed at pH 7 and at pH 9 at 25°C with a half-life of 12.5 hours and 1.21 hours, respectively, whereas it is supposed to be stable at pH 4 at 25°C. Melting point, boiling point, and vapour pressure are -80 °C, 172.5 °C, and 68 Pa (20 °C), respectively. Water solubility is ca. 24 g/100 mL at 20 °C, although it is not precisely measurable due to hydrolysis. Indirect photo-oxidation in the atmosphere by hydroxyl radicals is predicted to occur with a half-life estimated at 1.4 hours. This substance is readily biodegradable and has a low bioaccumulation potential based on its log Kow of 0.68. Fugacity modeling (Mackay level III) predicts that this substance if released to water is unlikely to migrate into other compartments. When this substance is released to air, 88.1 % stays in air and 11.9 % is transported into water and soil.

This substance has been tested in a limited number of aquatic species including algae, daphnids and fish. The toxicity results (growth inhibition: [OECD TG 201]) for algae (*Selenastrum capricornutum*) were 0.201 mg/L (72 h-EC50) and 0.01 mg/L (72 h-NOEC). A 72 h-EC50 of 0.23 mg/L and a NOEC of 0.039 mg/L was found in another green algae study (*Scenedesmus suspicatus*). The acute (immobility, OECD TG 202) and chronic (reproduction, OECD TG 211) toxicity results for daphnids (*Daphnia magna*) are 9.92 mg/L (48h-EC50), <5.00 mg/L (48h-NOEC), 3.94 mg/L (21d-LC50), 6.27 mg/L (21d-EC50), and 3.00 mg/L (21d-NOEC), respectively. The acute LC50 (96 hr, OECD TG 203) and prolonged LC50 (14 d, OECD TG 204) for fish (Medaka: *Oryzias latipes*) were 8.49 mg/L and 5.66 mg/L, respectively. Although this substance was hydrolyzed in these test conditions to acrylic acid and 2-dimethylaminoethanol readily, these results are, however, consistent with the aquatic toxicity of the metabolites reported in the respective SIARs. Toxicity of acrylic acid contributed to these results predominantly.

Exposure

The production volume of 2-dimethylaminoethyl acrylate was estimated at approximately 80,000 t/year world-wide in 2002 (6,000 t/year in Japan, 40,000 t/year in the USA, 34,000 t/year in the EU). This substance is produced in a closed system. Most of this substance is industrially converted to the quaternary ammonium salts. All of these salts are converted to the copolymers for flocculants to be used in water treatment and for paper industries (world-wide 95-97%). The remainder is used to produce other copolymers. The use of these polymers is almost exclusively limited to non-dispersive use and exposure to workers is low and the exposure to the general population is extremely unlikely.

During production and use of this substance, occupational exposure is possible by the inhalation and dermal route. The workplace exposures during those conversion processes are controlled by a closed equipment, ventilation and by personal protective equipments. Consumer exposure is controlled because the use of the substance is non-dispersive.

Because this substance hydrolyzes to acrylic acid and 2-dimethyaminoethanol in neutral or alkaline aquatic media, it can be assumed to hydrolyze in water under environmental exposure circumstances.
Migration of residual monomer from the polymer matrix is expected to be low.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

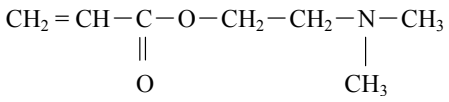
The chemical possess properties indicating a potential hazard for human health and the environment. Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 2439-35-2
IUPAC Name: 2-Dimethylaminoethyl acrylate
Molecular Formula: $C_7H_{13}NO_2$
Structural Formula:



Molecular Weight: 143.18
Synonyms: ADAME
Acrylate de dimethylaminoethyle
(Dimethylamino)ethylacrylat
Dimethylaminoethyl acrylate
2-Propenoic acid, 2-(dimethylamino)ethyl ester
Acrylic acid, 2-(dimethylamino)ethyl ester
DAA
N,N-dimethyl,N-(2-acryloxyethyl) amine
DMAEA
N,N-Dimethylaminoethyl acrylate

1.2 Purity/Impurities/Additives

Purity: equal to or more than 99 %w/w

Impurities:

2-dimethylaminoethnol: ca. 0.01 %W/W

acrylic acid: 0.01 %W/W

1.3 Physico-Chemical properties

2-Dimethylaminoethyl acrylate (ADAME) is a yellowish liquid with a pungent odor. Other physical-chemical properties are shown in table 1.

Table 1 Summary of physico-chemical properties

Property	Value
Physical state	
Melting point	-80 °C
Boiling point	172.5 °C
Relative density	0.94 g/cm^3 (25 °C)
Vapour pressure	68 Pa (20 °C)
Water solubility	ca. 24 g/100ml (20 °C) practically not measurable accurately due to hydrolysis
Partition coefficient n-octanol/water (log value)	0.68 (25 °C)

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production volume of 2-dimethylaminoethyl acrylate was estimated at approximately 80,000 t/y world-wide in 2002 (6,000 t/y in Japan, 40,000 t/y in the USA, 34,000 t/y in the EU). This substance is produced in a closed system. Most of this substance is industrially converted to quaternary ammonium salts. All of these salts are converted to the copolymers for flocculants to be used in water treatment. This substance is also used as a component monomer of copolymers in the polymer industry, and the products are used for paper industries. World-wide and in Japan, 95-97% of this substance is used to produce its quarternary ammonium salts which are used to produce polymers for industries such as water-treatment and paper-making. The remainder is used to produce other copolymers. The use of these polymers is almost exclusively limited to non-dispersive use and exposure to the general population is extremely unlikely.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

The Mackay level III fugacity model was employed to estimate the environmental distribution of this substance in air, water, soil and sediment. This was considered the key study and the results are shown below.

Table 2 Estimated distribution under three emission scenarios

Compartment	Release: 100 % to air	Release: 100 % to water	Release: 100 % to soil
Air	88.1 %	0.0 %	0.0 %
Water	3.6 %	100.0 %	1.1 %
Soil	8.4 %	0.0 %	98.9 %
Sediment	0.0 %	0.0 %	0.0 %

The results show that if this substance is released into water, 100.0 % stays in water, it is unlikely to migrate into other compartments. When this substance is released to air, 88.1 % stays in air and, 3.6 % is transported to water and 8.4 % to soil. If released into soil, 98.9 % stays in soil. However the calculation may include some uncertainty because of the weak dissociating property of this substance.

2.2.2 Photodegradation

Indirect photo-oxidation in air by hydroxy radicals is predicted to occur with a half-life estimated at 1.4 hrs (calculated using AOPWIN version 1.90, Syracuse Research Co.).

2.2.3 Stability in Water

Abiotically this substance is considered stable to hydrolysis in water at pH 4 at 25 °C, whereas it is hydrolyzed at pH 7 and pH 9 at 25 °C with half-lives of 12.5 and 1.21 hrs, respectively [CERI Japan, 1998]. This substance is hydrolysed to acrylic acid (AA, CAS No 79-10-7, see

corresponding SIDS Documents) and 2-dimethylaminoethanol (DMAE, CAS No 108-01-0, see corresponding SIDS Documents).

2.2.4 Biodegradation

This substance is readily biodegradable (OECD 301A and 301E: BOD = 96 % after 28 days) [ELF ATOCHEM 1993]. Similarly, a modified Zahn-Wellens test (OECD 302B) showed biodegradability of >95 % after 28 days [BASF, 1987]. These studies were conducted using industrial sludge. However the hydrolysis products acrylic acid and 2-dimethyaminoethanol are considered to be readily biodegradable (see corresponding SIDS Documents)

2.2.5 Bioaccumulation

This substance is considered to be of low bioaccumulative potential based on the log Kow (0.68 at 25 °C) [MITI Japan, 1993].

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposures at production sites may occur by the inhalation and dermal route.

There are 4 plants in Japan and this substance is produced in a fully-closed system. The atmospheric concentration was measured at one production site [Japan Industrial Safety and Health Association (JISHA), 2000]. The monitored data are shown in table 3.

Table 3 Workplace monitoring data for 2-dimethylaminoethyl acrylate

Operation	Monitoring data ppm	Frequency time/day	Working time hrs/time
maintenance	1.0 - 4.4	3	0.055
filling	below detection limit	12	0.5
laying	below detection limit	4	0.5
sampling	below detection limit	10	0.055
analysis	below detection limit	8	0.02

detection limit: 1 ppm

[Monitoring method]

The air sample was suctioned at the breathing zone of the worker and adsorbed through an absorbent (XAD-2: porous polymer) and desorbed with a solvent (butyl acetate) and analyzed by GC.

As shown in table 3, the monitored exposure concentrations were below 25.7 mg/m^3 (4.4 ppm) at the maintenance work. The daily intake (respiratory EHEinh) for a worker (body weight; 70 kg, respiratory volume; 1.25 m^3/hr) without protection is calculated as 0.077 mg/kg/day. The duration of dermal exposure is assumed to be 0.50 hr/day. EHEder for the worker is calculated as 1.2 mg/kg/day, assuming that the work is classified as non-dispersive, direct handling, and contact level is incidental. Normally, workers wear protections for eye/face, skin and respiratory tract during the work in well-ventilated situations.

Occupational Exposure Limit of 2-Dimethylaminoethyl acrylate

There is no available official recommendation. The occupational exposure control limit at the production site is recommended as TLV-TWA (VME) = 2.9 mg/m^3 (0.5 ppm), TLV-STEL (VLE) = 5.8 mg/m^3 (1 ppm).

2.3.2 Consumer Exposure

This substance is not considered to be contained in consumer products in Japan and even world-wide , because most of this substance is industrially converted to the quaternary ammonium salt and polymerized to form flocculants to be used in water treatment. This substance is also used as a component monomer for the production of copolymers in the polymer industry, and the products are used for paper industries. World-wide and in Japan, 95-97% of this substance is used to produce its quarternary ammonium salts which are used to produce polymers for industries such as water-treatment and paper-making. Migration of residual monomer as acrylic acid and 2-dimethyaminoethanol from the polymer matrix is expected to be low, because this substance has a low bioaccumulation potential and is readily biodegradable.

2.3.3 Indirect exposure via the environment

The production volume of 2-dimethylaminoethyl acrylate was estimated at approximately 80,000 t/y world-wide in 2002 (6,000 t/y in Japan, 40,000 t/y in the USA, 34,000 t/y in the EU). This substance is produced in a closed system. Release of residual chemical from polymer flocculant can be assumed to occur as acrylic acid and 2-dimethyaminoethanol in water due to a fast hydrolysis of this substance., The indirect exposure to humans via the environment of these compounds are limited due to their biodegradability and low bioaccumulation potential. Effect of exposure may be limited to local settings, because of the biodegradability of these compounds.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

There is no available information specific to 2-dimethylaminoethyl acrylate. Based on the fact that the structurally related compound 2-dimethylaminoethyl methacrylate hydrolyzes in simulated saliva and simulated intestinal fluid to methacrylic acid and dimethylaminoethanol, it can be assumed that this substance hydrolyzes to acrylic acid and dimethylaminoethanol in the same circumstances. This is supported by the comparison of acute toxicities between acrylic acid with methacrylic acid and this substance with 2-dimethylaminoethyl methacrylate.

3.1.2 Acute Toxicity

There are various study results available on the acute toxicity by different administration routes. Fourteen reports on the acute toxicity via oral, dermal, inhalation or other routes to rats, mice or rabbits were reviewed and summarized in the table 4 shown below.

Table 4 Acute toxicity of 2-dimethylaminoethyl acrylate in experimental animals

Route	Animals	Values	Type	References	Method
Oral	Rat	455 mg/kg bw	LD50	Atochem, 1989b	OECD TG 401
Dermal	Rat	419 mg/kg bw	LD50	Atochem, 1989c	OECD TG 402
Dermal	Rat	891 mg/kg bw	LD50	Allied Colloids	OECD TG 402
Dermal	Rabbit	50 - 200 mg/kg bw	LD50	BASF AG, 1979	Unknown
Inhalation/4hrs	Rat	0.066 mg/L	LC50	Atochem, 1991a	OECD TG 403
Inhalation/4hrs	Rat	< 0.352 mg/L	LC100	Atochem, 1991b	OECD TG 403
Inhalation/1hr	Rat	0.972 mg/L	LC50	Atochem, 1991c	OECD TG 403
Inhalation/4hrs	Rat	0.22 mg/L	LC50	BASF AG, 1979	OECD TG 403
Inhalation/4hrs	Rat	> 0.06 mg/L	LC50	Atochem, 1992	OECD TG 403
i.p.	Rat	183 mg/kg bw	LD50	Rowell, 1976d	Unknown
i.p.	Mouse	200 mg/kg bw	LD50	BASF AG, 1979	Unknown

Inhalation

Regarding acute inhalation toxicity, the study by Atochem (1991a) was considered to be the most reliable and identified as the key study because it was well conducted according to OECD TG 403 and in compliance with GLP. SD rats (No. of animal/group/sex: 5) were exposed to concentrations of 0 (control), 0.037, 0.058, 0.092 and 0.460 mg/L for 4 hrs. Toxicity was recognized within a few days after dosing. Minimal vascular congestion and areas of pulmonary edema were found in lungs of the decedents. The acute inhalation toxicity LC_{50} is considered to be 0.066 mg/L (aerosol). Although no histopathological data are available, due to lung weight to body weight ratio, the substances would cause irritation or corrosion to the respiratory tract if inhaled.

Dermal

Regarding acute dermal toxicity, the study on rats by Atochem(1989c) was conducted in accordance with OECD TG 402 and in compliance with GLP and identified as the key study. SD

rats (No. of animal/group/sex: 5) were administered doses of 200, 330, 500, 700, 980, 1400 and 2000 mg/kg. Mortality was noted principally within one day after dosing. Necropsies did not reveal any abnormalities cutaneous effects at the site of application. No sex-related toxicity was observed. The acute dermal toxicity LD_{50} is considered to be 419 mg/kg bw.

Oral

Regarding acute oral toxicity, the study byAtochem (1989b) was considered to be the most reliable and identified as the key because this study was well conducted according to OECD TG 401 and in compliance with GLP. SD rats (No. of animal/group/sex: 5) were administered doses of 0 (vehicle), 80, 160, 320, 640 and 2000 mg/kg. Mortality was noted principally within one day after dosing. Necropsies did not reveal any significant gross lesions. No sex-related differences in toxicity were noted. The oral acute toxicity LD_{50} is considered to be 455 mg/kg bw.

Other Routes of Exposure

As to the acute toxicity by intraperitoneal administration (i.p.), two values were reported in rats and in mouse. The severer value was 183 mg/kg bw for rats [Rowell, 1976d].

Conclusion

(Oral toxicity) Based on mortality data at doses of 80 - 2000 mg/kg, the acute oral LD_{50} of this substance is considered to be 455 mg/kg bw. Toxicity was recognized immediately after dosing.

(Dermal toxicity) Based on mortality data at doses of 200 - 2000 mg/kg, the acute dermal LD_{50} of this substance is considered to be 419 mg/kg bw. Toxicity was recognized immediately after dosing.

(Inhalation toxicity) Based on mortality data at concentrations of 0.037 - 0.460 mg/L, the acute inhalation LC_{50} of this substance is considered to be 0.066 mg/L.

3.1.3 Irritation

The summaries of the study results are shown in the table 5 below.

Table 5 Summary of other human health related information

Species	Method	Result	Reference
Irritation (skin)			
Rabbit	Draize test	Corrosive Primary irritation score: 8.0	Atochem, 1981
Rabbit	OECD TG 404 Acute Dermal Irritation/Corrosion	Corrosive (causes burns)	Potokar, 1985
Rabbit	Draize test	Corrosive. Primary irritation index = 7.6 (91/12)	BASF AG, 1979
Irritation (eye)			
Rabbit	Federal Register (USA)-29 FR13009, 1964	Irritating (highly)	Atochem, 1981
Rabbit	Draize test	Corrosive	BASF AG, 1979

Skin Irritation

There are four reports available. Among them, the study by Atochem (1981) was identified as the key study because it was conducted by the recommendations of the Federal Hazardous Substances Labelling Act Regulations, Section 191.11, published in the Federal Register (USA)-29 FR13009, 1964 [. This substance was applied to the intact and abraded skin of New-Zealand White rabbits at the dose level of 0.5 ml per animal under an occlusive patch for 24 hrs. The cutaneous reactions were observed after the removal of the patch and after 72 hrs. Severe erythema, turgor, discoloration, tissue destruction and blacking characterised the reactions exhibited 24 and 48 hrs following application. A primary irritation score of 8.0 was obtained. Under these test conditions, this substance was considered to be corrosive to the skin.

Eye Irritation

There are two reports available. The study by Atochem (1981) was identified as the key study because it was conducted by the recommendations of the Federal Hazardous Substances Labelling Act Regulations, Section 191.11, published in the Federal Register (USA)-29 FR13009, 1964. Severe cornea, iris and conjunctive lesions were displayed in all animals within 1 hr after the instillation of 0.1ml this substance. This substance was considered as severely irritant to eyes.

3.1.4 Sensitisation

One study was located. The sensitizing potential of this substance was evaluated on albino guinea pigs according to a modified Magnusson and Kligman maximization test. Cutaneous reactions likely to be caused by the sensitization potential of this substance were observed.

3.1.5 Repeated Dose Toxicity

Two studies have been located. Both of them were oral administration studies. One study was conducted according to OECD TG 422 in compliance with GLP [MHW Japan, 1998], and the other was conducted according to OECD TG 408 in compliance with GLP [Atochem, 1999]. Both studies were identified as key studies. The two studies are summarized below.

1) MHW, Japan: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test

According to the OECD test guidelines for combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], SD (Crj: CD) rats (12 animal/group/sex) were administered the doses of 0 (vehicle; corn oil), 4, 20, and 100 mg/kg/day by gavage. The dosing period for males was 43 days, and females were dosed from 14 days before mating to day 3 of lactation. The results were summarized below.

At 100 mg/kg/day group, two females died. Males showed a transient suppression of body weight gain and a decrease in food consumption. At necropsy, thickening of the wall of the forestomach and enlargement of the pancreatico-duodenal lymph nodes were observed in both sexes. At histopathology, ulceration, inflammatory cell infiltration and hyperplasia of the mucosa in the forestomach and hyperplasia of plasma cells in the pancreatico-duodenal lymph nodes were observed in both sexes. Additionally, atrophy of the thymus was observed in females. At hematology and blood chemistry, increased ratios in reticulocyte, platelet and segmented neutrophil counts and decrease in albumin were observed in males. At 20 mg/kg/day, ulceration, inflammatory cell infiltration and hyperplasia of the mucosa in the forestomach were observed in 2 males. However, these changes were not statistically significant, and considered not toxicologic.

No effects were observed at 20 mg/kg/day in females and at 4 mg/kg/day. The NOAEL for the repeat dose toxicity is considered to be 20 mg/kg/day for both sexes.

2) Atochem: Repeated Dose 90-Day Oral Toxicity Study in Rodents

According to the OECD test guidelines for repeated dose 90-day oral toxicity study in rodents [OECD TG 408], SD (Crl: CD) rats were administered doses of 0 (vehicle; peanut oil), 2, 10, and 50 mg/kg/day by gavage. The dosing period for males and females was 13 weeks. The results are summarized below.

Twenty rats/sex were used in the control group, 10 rats/sex in the low- and intermediate dose-levels and 25 rats/sex in the high dose-level. Non-sporadic death or imminent death occurred at 50 mg/kg/day in 13 males and 9 females. Twenty-one of these deaths (except one male) occurred during the exposure period. The cause of death was lung lesions, which were considered to be due to direct irritation from regurgitated stomach contents. No clinical signs related to this compound were observed at 2 and 10 mg/kg/day. Ptyalism and/or loud breathing were observed in a few animals at 50 mg/kg/day. However, it was transient and the animals recovered. Therefore, it was considered to be unrelated to this compound. There were no effects at 2 and 10 mg/kg/day. There was an increase in neutrophil counts and a decrease in lymphocyte counts at hematology at 50 mg/kg/day. There were no changes in absolute and relative organ weight. There were no effects at food consumption, ophthalmology, blood biochemistry and urinalysis.

Macroscopic examination: At 50 mg/kg/day, the following changes, considered to be related to treatment, were seen in decedents and animals that survived the treatment period: greyish foci in the mucosa of the forestomach in 11/20 males and 13/19 females, enlargement of the pancreatic lymph nodes in 5/20 males and 6/19 females, dilatation or reddish color of the lungs 7/20 males and 6/19 females. None of above findings was seen in animals killed at the end of the recovery period. There were no effects of treatment on any of the tissues examined in males or females at 2 or 10 mg/kg/day. Microscopic examination: At 50 mg/kg/day, the following changes, considered to be related to treatment, were seen in decedents and surviving animals after 13 weeks treatment: ulceration, hyperplasia/hyperkeratosis, infiltration or granulation tissue formation in the submucosa, edema in mucosa and submucosa and necrosis of the mucosa/submucosa in forestomach, alveolar haemorrhage or edema and congestion in lungs. At 10 mg/kg/day, hyperplasia/hyperkeratosis and edema and inflammatory cell infiltration (all due to direct irritation of this substance) of the forestomach submucosa were seen in 4 males. These findings were almost of minimal grade which were not regarded to be adverse effect. The NOAEL for the repeat dose toxicity is considered to be 10 mg/kg/day for both sexes.

Conclusion

From the two above-mentioned examinations, the findings at or more than 50 mg/kg/day were considered toxicologically significant. This substance was not toxic at 20 mg/kg/day in both sexes in the combined study. Nevertheless, the NOAEL was considered to be 10 mg/kg/day in the 90-day study, by the author.

3.1.6 Mutagenicity

Five reports were reviewed and summarized in table 6 shown below. These were two bacterial *in vitro* test reports, two non-bacterial *in vitro* test reports and one genotoxic *in vivo* test report.

Table 6 Summary of genotoxicity studies

Type of test	Test system	Dose	Result	Reference
Bacterial in vitro test				
Reverse mutation TG 471 and 472	Salmonella typhimurium (strains TA100, TA1535, TA98, TA1537) Escherichia coli (strain WP2 uvrA)	Up to 5000 ug/plate	With MA: Positive in TA98. Negative for all the other strains at all doses	MHW Japan, 1997
		Up to 2500 ug/plate (TA98, TA1537) Up to 5000 ug/plate (TA100, TA1535, WP2 uvrA)	Without MA: Negative for all strains at all doses	
	S. typhimurium (strains TA100, TA1535, TA98, TA1537)	Up to 10000 ug/plate	Negative (+ and - MA)	Zeiger et al, 1987
Non-bacterial in vitro test				
Chromosomal aberration test TG 473	CHL/IU cells	Up to 0.050 mg/ml (+ MA), 0.010 mg/ml (- MA): (short-term treatment)	Positive (clastogenicity and polyploidy) (+ and - MA)	MHW Japan, 1997
		Up to 0.060 mg/ml: (continuous treatment)	Positive (clastogenicity and polyploidy) (- MA)	
	Human lymphocytes	Up to 156 mg/ml	Positive (+ and - MA)	Atochem, 1991d
Genetic in vivo test				
Micronucleus Test TG 474	Mice (i. p.)	75 mg/kg bw, two administrations, 24 hrs interval Time of sacrifice: 24 and 48 hrs after the 2nd administration	Negative	Atochem, 1993

* MA: Metabolic activation

In vitro Studies

Bacterial test

Two studies were reviewed. The study by MHW Japan (1997) was conducted according to the guidelines for screening mutagenicity of testing of chemicals and reverse mutation assay [OECD TG 471 and TG 472] in compliance with GLP. The other report was reliable. Both studies were identified as key studies. The two studies were summarized below.

1) MHW, Japan (1997): Bacterial Reverse Mutation Assay

The test was conducted two times for all cells with and without rat S9, and the results were negative except for a marginal response in one strain of *S. typhimurium* TA 98 with metabolic activation. Then the confirmation test was conducted, but no reproducibility was observed. These marginal

responses seemed not biologically significant. Toxic effects were observed at 1250 ug/plate (TA98, TA1537), 2500 ug/plate (TA1535), and 5000 ug/plate (TA100, WP2*uvr*A) without metabolic activation, and 2500 ug/plate (TA1535), 5000 ug/plate (TA100, TA98, TA1537) with metabolic activation. Toxic effects were not observed for WP2*uvr*A with metabolic activation.

2) Zeiger et al. (1987): Ames Test

Zeiger et al. (1987) reported that this substance was negative in any of *S. typhimurium* TA98, TA100, TA1535 and TA1537 at the doses of 10 to 10,000 ug/plate with hamster S9, with rat S9 and without metabolic activation. Toxic effects were observed at 3333 ug/plate (TA98, TA100), 1000 ug/plate (TA1535, TA1537) with and without S9.

Non-bacterial *in vitro* test

Two studies were reviewed. Two studies were chromosomal aberration tests *in vitro* by guidelines for screening mutagenicity of testing of chemicals and *in vitro* mammalian cytogenetic test [OECD TG 473] with cultured Chinese hamster lung cells (CHL/IU) [MHW Japan, 1997] and human lymphocytes [Atochem, 1991d]. The study by MHW Japan (1997) was conducted in compliance with GLP and was identified as the key study. The summary and data of the study are shown below.

Table 7 Chromosomal aberrations assay on cultured Chinese hamster lung cells

Treatment	S9	Concen-tration (ug/ml)	Incidence (%) of cells with aberrations including gap	Judgment on structural aberration	Incidence (%) of cells with polyploid	Judgment on numerical aberration	Concentration (ug/ml) observed cytotoxicity
24 hrs continuous	without	60	23.5	+	10.75	+	120
48 hrs continuous	without	60	8.5	+	6.21	+	120
6 hrs short-term	without	10	16.0	+	10.88	+	20
6 hrs short-term	with	50	12.5	+	5.25	+	100

Based on these results, this substance is considered to induce chromosomal aberrations, which were mainly the chromatid exchanges, and polyploidy with and without metabolic activation. However, the aberrations are weak even at the highest concentrations.

The study of Atochem with human lymphocytes showed weak positive results at the highest concentrations.

In vivo Studies

One study on the micronucleus test was reviewed. The study was conducted according to OECD TG 474 in compliance with GLP and was identified as the key study [Atochem, 1993]. The summary of the study is shown below.

Atochem (1993): on the clastogenic potential of this substance in OF1 mice

The animals (5 males and 5 females per group) received two administrations separated by 24 hrs, of this substance at one dose of 75 mg/kg which was the MTD (maximum tolerated dose) for each

time by the intraperitoneal route. Cyclophosphamide at the dose level of 25 mg/kg (two times i.p. injection) served as the positive control. The test animals were killed at 24 and 48 hrs after the 2nd administration and the bone marrow smears were examined for the presence of the micronuclei in 2000 polychromatic erythrocytes per mouse and for the PCE/NCE ratio. The number of the micronucleated polychromatic cells in the dosed animals was not significantly different from that of the animals in the control groups. A decrease in the P/N ratio was observed indicating that the test substance had actually reached the bone marrow. This substance did not induce cytogenetic damage to the bone marrow cells of mice in this test.

Conclusion

This substance did not induce gene mutations in 3 strains of *S. typhimurium* and in *E. coli* but did induce gene mutations in the TA98 strain with metabolic activation in one out of two studies. *In vitro*, this substance was only weakly positive in the highest dose tested in CHL lung cells and human lymphocytes with and without metabolic activation. However, *in vivo*, this substance was negative when administered i.p. at the MTD in a single dose study. Based on the present results, and taking into account data on structurally related substances, it is unlikely that this substance is mutagenic *in vivo*. Based on mutagenicity data, this substance would not be expected to be carcinogenic.

3.1.7 Carcinogenicity

There is no carcinogenicity data. Based on mutagenicity data, this substance would not be expected to be carcinogenic.

3.1.8 Toxicity for Reproduction

Two studies have been located. There was one combined repeated dose toxicity study with the reproduction/developmental toxicity screening test report by MHW Japan (1997) and one teratogenicity test report by Atochem (1997). The first study was conducted according to OECD TG 422 in compliance with GLP [MHW Japan, 1997], and the other one was conducted according to OECD TG 414 in compliance with GLP [Atochem, 1997]. Both studies were identified as key studies. The two studies are summarized below.

1) MHW, Japan (1997): Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test

According to the OECD test guideline for combined repeat dose and reproduction/developmental toxicity screening [OECD TG 422], SD (Crj: CD) rats (12 animal/group/sex) were administered the doses of 0 (vehicle; corn oil), 4, 20, and 100 mg/kg/day by gavage. The dosing period for males was 43 days, and females were dosed from 14 days before mating to day 3 of lactation.

Two dams died at 100 mg/kg/day. In inspection of parent animals, reproductive parameters as the mating index, the fertility index, number of corpora lutea or implantations, the implantation index, the gestation index, the delivery index, gestation length, parturition or maternal behavior were not affected by the compound. In inspection of neonates, there were no changes related to the compound in number of offspring, the sex ratio, the live birth index, the viability index or body weight.

No abnormal findings were observed at external features, clinical signs or necropsy. Therefore, it is thought that there are no effects of the compound on the reproductive and developmental parameters. The NOAEL for reproduction/developmental toxicity is considered to be 100 mg/kg/day.

2) Atochem (1997): Teratogenicity Test

According to the OECD test guideline 414, SD (Crl: CD) rats were administered the doses of 0 (vehicle; peanut oil), 10, 30 and 100 mg/kg/day (25 animal/group) by gavage. Females were dosed from day 6 to day 15 after mating.

Maternal effects: One female was killed moribund at 100 mg/kg/day, two females died at 30 mg/kg/day. Some clinical signs (principally loud breathing, piloerection, chromorhinorrhea, round back and dyspnea) were observed in 17/25 females at 100 mg/kg/day and in 8/25 females at 30 mg/kg/day. No abortions occurred in any female. No total resorptions occurred in any female except one at 100 mg/kg/day. The food consumption and body weight gain at 100 mg/kg/day were lower than those of the control. In macroscopic examinations, at 30 and 100 mg/kg/day, gaseous dilatation or thickening of mucosa in gastrointestinal tracts were observed in 3/25 and 6/25 females, respectively. These findings were principally observed in the decedent animals. There were no effects at 10 mg/kg/day. This substance was maternally toxic at 30 mg/kg/day.

Developmental effects: The post-implantation loss was increased and the body weight of the fetuses was decreased at 100 mg/kg/day. The number of live fetuses and sex-ratio were not affected. No effect was observed at 10 and 30 mg/kg/day. In external examination, 27/299 fetuses showed anomalies (14 fetuses from the same litter were dwarf, 13 other fetuses from another litter had adactyly) at 100 mg/kg/day. In internal examination, 2/144 fetuses showed anomalies (one fetus had a cleft palate, other fetuses presented hydrocephaly, and six dwarf fetuses suffered testicular ectopia). The absence of ossification of various bones (vertebrae, sternebrae) were found in many individuals. As fetal variations, reduced ossification of many bones (head, vertebrae, sternebrae, limbs) were found and the incidence for the reduced of ossification of 6th sternebra was increased at 100 mg/kg/day. At 30 mg/kg/day, reduced ossification of head and vertebrae were found. The NOAEL for teratogenicity is delineated at 30 mg/kg/day.

Conclusion

No prenatal developmental effects were observed in the combined reproduction/toxicity study (OECD TG 422). In the teratology study, the NOAEL for maternal toxicity in rats was 10 mg/kg. Prenatal developmental toxicity was only observed at doses (100 mg/kg) which produced signs of maternal toxicity and mortality. The NOAEL for reproduction/developmental toxicity and teratogenicity are considered to be 10 and 30 mg/kg/day, respectively.

3.2 Initial Assessment for Human Health

There is no metabolism data specific to this substance. However, based on the fact that the structurally related compound 2-dimethylaminoethyl methacrylate hydrolyzes in simulated saliva and simulated intestinal fluid to methacrylic acid and dimethylaminoethanol, it can be assumed that this substance hydrolyzes to acrylic acid and dimethylaminoethanol in the same circumstances. This is supported by the comparison of acute toxicities between acrylic acid with methacrylic acid and this substance with 2-dimethylaminoethyl methacrylate.

The acute oral LD_{50}, dermal LD_{50}, and inhalation LC_{50} in rats are 455 mg/kg, 419 mg/kg, and 0.066 mg/L (aerosol), respectively, which indicates a higher dermal/inhalation toxicity than oral. This substance is considered to be severely irritating or corrosive to skin and eye in rabbits. This substance does have a sensitizing potential.

A repeated dose 90-day oral toxicity study in rodents [OECD TG 408] was conducted with SD (Crl: CD) rats at 0, 2, 10 and 50 mg/kg/day administered by gavage. At 50 mg/kg/day, the macroscopic lesions were limited to sporadic lung damage that was caused by reflux of stomach content. Judging from the hyperplasia/keratosis or other irritation changes found in forestomach, the reflux

is a result of incontinence in the gastro-intestinal tract. This substance was not toxic at 2 and 10 mg/kg/day. At the latter dose-level, treatment-related lesions were found in the forestomach of 4 males, however, these findings were almost of minimal grade which were not regarded to be adverse effects. A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] was also available with SD (Crj: CD) rats at doses of 0, 4, 20 and 100 mg/kg/day administered by gavage. The toxicity revealed is common in the two studies. At 100 mg/kg/day, similar changes compared to those seen at 50 mg/kg/day in the former study was observed. At 20 mg/kg/day, similar changes in the forestomach were observed in 2 males. However, these changes were not statistically significant, and considered to be not toxicologic by the authors. This substance was not toxic at 20 mg/kg/day in both sexes in the combined study. Nevertheless, the NOAEL was considered to be 10 mg/kg/day in the 90-day study, by the author.

This substance did not induce gene mutations in 3 strains of *Salmonella typhimurium* and in *Escherichia coli* but did induce gene mutations in the TA98 strain with metabolic activation in one out of two studies. *In vitro*, this substance was only weakly positive in the highest dose tested in CHL lung cells and human lymphocytes with and without metabolic activation. However, *in vivo*, this substance was negative when administered i.p. at the MTD in a single dose study. Based on the present results, and taking into account data on structurally related substances, it is unlikely that this substance is mutagenic *in vivo*. Based on mutagenicity data, this substance would not be expected to be carcinogenic.

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] (0, 4, 20, 100 mg/kg/day) was conducted with SD (Crj: CD) rats. There was no sign of reproductive or developmental toxicity up to 100 mg/kg/day, but maternal toxicity was overt and included death. Furthermore, a teratogenicity study [OECD TG 414] (0, 10, 30, 100 mg/kg/day) were conducted with SD (Crl: CD) rats. At 100 mg/kg/day, 27/299 fetuses showed anomalies (dwarf, adactyly) in external examination and 2/144 fetuses showed anomalies (cleft palate, hydrocephaly, testicular ectopia) in internal examination. The absence of ossification of various bones (vertebrae, sternebrae) was found in many individuals. Maternal toxicity including death was evident. At 30mg/kg/day, no teratogenic effects were observed, two females, however, died and this substance was found maternally toxic. Fetuses with reduced ossification were found at this dose. At 10 mg/kg, no adverse effect was evident. In the teratology study, the NOAEL for maternal toxicity in rats was 10 mg/kg. Prenatal developmental toxicity was only observed at doses (100 mg/kg) which produced signs of maternal toxicity and mortality. The NOAEL for reproduction/developmental toxicity and teratogenicity are considered to be 10 and 30 mg/kg/day, respectively.

Other Valid and Reliable Information

2-Dimethylaminoethyl methacrylate (MADAME) [CAS No.: 2867-47-2]

2-Dimethylaminoethyl acrylate (ADAME) belongs to esters of acrylic acid. 2-Dimethylaminoethyl methacrylate (MADAME) has the same alcohol moiety as ADAME and the acid moiety has an additional methyl group on it. That makes some degree of difference with ADAME from MADAME of the analogues in the toxicological feature. The most substantial difference is the potential of sensitization demonstrated on ADAME in the maximization test by Magnusson and Kligman. Although ADAME shows more stringent (strict) effects in other aspects, the findings (information) on MADAME may be extrapolated to ADAME.

MADAME has been assessed previously in the OECD HPV Chemicals Programme and the document includes more information than ADAME (see SIAR of MADAME, CAS-No 2867-47-2). According to the initial assessment of MADAME, this substance is metabolized by local tissue

esterase, or hydrolysed in alkaline or neutral aqueous media. ADAME may be presumed to undergo in the same metabolic pathway. It is irritating to tissues directly in contact.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

2-Dimethylaminoethyl acrylate has been tested in a limited number of aquatic species. Results are summarized in table 8. All the data, except that for golden ide (*Leucisuc idus*), were derived from experiments conducted under GLP. And, the lowest chronic test result was 0.01 mg/L (*Selenastrum capricornutum* 72 h (nc) NOEC).

Table 8 Summary of effects of 2-dimethylaminoethyl acrylate on aquatic organisms

Organism	Test duration	Result (mg/L)	Reference
Algae			
Green alga (Selenastrum capricornutum)	72 h (s)	EC50 (bms) = 0.201 (nc) NOEC (bms) = 0.01 (nc) EC50 (rate) > 1.00 (nc) NOEC (rate) = 0.01 (nc)	MOE, Japan 1997d
Green alga (Scenedesmus subspicatus)	72 h (s)	EC50 (bms) = 0.23 (nc) NOEC (bms) = 0.039 (nc) EC50 (rate) = 0.88 (nc)	BASF AG, 1988
Invertebrates			
Water flea (Daphnia magna)	48 h (ss)	EC50 (imm) = 9.92 (nc) NOEC (imm) < 5.00 (nc)	MOE, Japan 1997b
	21 d (ss)	LC50 = 3.94 (nc) EC50 (rep) = 6.27 (nc) NOEC (rep) = 3.00 (nc) LOEC (rep) = 10.00 (nc)	MOE, Japan 1997e
Fish			
Medaka (Oryzias latipes)	96 h (ss)	LC50 = 8.49 (nc)	MOE, Japan 1997a
	14 d (ss)	LC50 = 5.66 (nc) LC0 = 10.0 (nc) NOEC = 1.00 (nc)	MOE, Japan 1997b
Golden ide (Leucisuc idus)	96 h (s)	LC50 = 10 - 22 (nc) NOEC = 4.6 (nc)	BASF AG, 1987

s: static ss: semi-static nc: nominal concentrations bms: biomass imm: immobilization
rep: reproduction

Toxicity to green alga is of uniquely low value (toxic) for NOEC and high value in EC50, which is qualitatively similar to the toxicity of acrylic acid. This substance was hydrolyzed in these test conditions to acrylic acid and 2-dimethylaminoethanol readily. The toxicity of acrylic acid probably contributed predominantly to these results.

4.2 Terrestrial Effects

There is no available information.

4.3 Other Environmental Effects

There is no available information.

4.4 Initial Assessment for the Environment

Abiotically 2-dimethylaminoethyl acrylate is hydrolyzed at pH 7 and at pH 9 at 25°C with a half-life of 12.5 hrs and 1.21 hrs, respectively, whereas it is supposed to be stable at pH 4 at 25°C. Melting point, boiling point, and vapour pressure are -80 °C, 172.5 °C, and 68 Pa (20 °C), respectively. Water solubility is ca. 24 g/100mL at 20 °C, although it is not measurable due to hydrolysis. Indirect photo-oxidation in atmosphere by hydroxy radicals is predicted to occur with a half-life estimated at 1.4 hrs. This substance is readily biodegradable and has a low bioaccumulative potential based on its log Kow of 0.68 at 25 °C. The results of a generic fugacity model (Mackay level III) show that if this substance is released into water, 100.0 % stays in water. When this substance is released to air, 88.1 % stays in air, 3.6 % is transported to water, and 8.4 % is transported to soil. If released into soil, 98.9 % stays in soil.

This substance has been tested in a limited number of aquatic species including algae, daphnids and fish. The toxicity results (growth inhibition: [OECD TG 201]) for algae (*Selenastrum capricornutum*) were 0.201 mg/L (72 h-EC_{50}) and 0.01 mg/L (72 h-NOEC). The acute (immobility: [OECD TG 202]) and chronic (reproduction: [OECD TG 211]) toxicity results for daphnids (*Daphnia magna*) are 9.92 mg/L (48h-EC_{50}), <5.00 mg/L (48h-NOEC), 3.94 mg/L (21d-LC_{50}), 6.27 mg/L (21d-EC_{50}), and 3.00 mg/L (21d-NOEC), respectively. The acute LC_{50} (96 hrs: [OECD TG 203]) and prolonged LC_{50} (14 d: [OECD TG 204]) for fish (Medaka: *Oryzias latipes*) were 8.49 mg/L and 5.66 mg/L, respectively. Although this substance was be hydrolyzed in these test conditions to acrylic acid and 2-dimethylaminoethanol readily, these results are, however, consistent with the aquatic toxicity of the metabolites reported in the respective SIARs. Toxicity of acrylic acid contributed to these results predominantly.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possess properties indicating a potential hazard for human health and the environment. Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work.

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SIDS Dossier

Existing Chemical	:	ID: 2439-35-2
CAS No.	:	2439-35-2
EINECS Name	:	2-(Dimethylamino)ethyl acrylate
EINECS No.	:	219-460-0
TSCA Name	:	2-Propenoic acid, 2-(dimethylamino)ethyl ester
Molecular Formula	:	C7H13NO2

Producer Related Part

Company	:	NIPPON SHOKUBAI CO., LTD
Creation date	:	04.10.2001

Substance Related Part

Company	:	NIPPON SHOKUBAI CO., LTD
Creation date	:	04.10.2001
Memo	:	ATOFINA as Data Contribution Company
Printing date	:	04.02.2003 including Robust summary
Revision date	:	16.05.2003
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Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

Type : lead organisation
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Cedex :
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Country : Japan
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Telefax : 81-3-3597-7353
Telex :
Cedex :
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
01.10.2002

Type : Other
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Partner :
Date :
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Telefax : 49-621-60-86-08-268
Telex :
Cedex :
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
01.10.2002

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

Name of recipient : Mr.Koji Tomita, Ministry of Foreign Affairs, Economic Affairs Bureau, Second International Organizations Div.
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Telefax : +81-3-3581-9470
Telex :
Cedex :
01.10.2002

1.1 GENERAL SUBSTANCE INFORMATION

Substance type : Organic
Physical status : Liquid
Purity : >= 99 % w/w
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
01.10.2002

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

Type of spectra : NMR
Source : Beilstein Online [2001]
03.01.2002 (36)

Type of spectra : IR
Source : Beilstein Online [2001]
03.01.2002 (1)

1.2 SYNONYMS

ADAME ; Acrylate de dimethylaminoethyle
ADAME : ATOFINA's Tradename
Source : Atofina SA Paris la Défense
20.03.2003

(Dimethylamino)ethylacrylat
Source : BASF AG Ludwigshafen
28.09.1994

2-Propenoic acid, 2-(dimethylamino)ethyl ester

Source : BASF AG Ludwigshafen
28.09.1994

Acrylic acid, 2-(dimethylamino)ethyl ester
Source : SNF S.A. Saint-Etienne
BASF AG Ludwigshafen
04.06.1998

DAA: Dimethylaminoethyl acrylate, 2-dimethylaminoethyl acrylate ; N,N-dimethyl,N-(2-acryloxyethyl) amine
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
SNF S.A. Saint-Etienne
BASF AG Ludwigshafen
20.03.2003

DMAEA; N,N-Dimethylaminoethyl acrylate; Acrylic acid, 2-(Dimethylamino)ethyl ester; Dimethylaminoethyl acrylate; 2-Propenoic acid, 2-(Dimethylamino)ethyl ester
Source : Allied Colloids Ltd. Bradford
CIBA SPECIALTY CHEMICALS INC. Basel
06.05.1994

1.3 IMPURITIES

CAS-No : 79-10-7
EINECS-No : 201-177-9
EINECS-Name : acrylic acid
Contents : 0.01 % w/w
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Test substance : NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
03.01.2002 (44)

CAS-No : 108-01-0
EINECS-No : 203-542-8
EINECS-Name : 2-dimethylaminoethanol
Contents : ca. 0.01 % w/w
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Test substance : NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
04.04.2002 (44)

Purity : Other
CAS-No :
EC-No :
EINECS-Name : Water
Molecular formula : H20
Value : <= .2 % w/w
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Purity : typical for marketed substance
CAS-No : 108-01-0
EC-No : 203-542-8
EINECS-Name : 2-dimethylaminoethanol
Molecular formula :
Value : <= .03 % w/w
Source : Atofina SA Paris la Défense
22.05.2003

1.4 ADDITIVES

CAS-No : 150-76-5
EINECS-No : 205-769-8
EINECS-Name : mequinol
Contents : ca. 0.2 % w/w
Remark : Synonym :Methoquinone
Function:inhibitor of polymerization
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Test substance : NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
01.10.2002 (44)

Purity : typical for marketed substance
CAS-No : 108-01-0
EC-No : 203-542-8
EINECS-Name : 2-dimethylaminoethanol
Molecular formula :
Value : <= .03 % w/w
Source : Atofina SA Paris la Défense
22.05.2003

CAS-No :
EINECS-No :
EINECS-Name : hydroquinone derivative
Contents : < 0.1 % w/w
Source : Atofina SA Paris la Défense
07.04.2002 (55)

1.5 QUANTITY

Quantity : ca. - 8000 tonnes produced in 2002
Remark : Worldwide production in 2002 = 80000 tonnes
USA 40000t, Europe 34000t, Japan 6000t
Source : Atofina SA Paris la Défense
23.05.2003

Quantity : 5,000 t/y in Japan and 58,000 t/y world-wide in 2000
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
20.12.2002

1.6.1 LABELLING

Labelling : provisionally by manufacturer/importer
Specific limits : no
Symbols : T+, , ,
Nota : , ,
R-Phrases : (26) Very toxic by inhalation
(21/22) Harmful in contact with skin and if swallowed
(34) Causes burns
(43) May cause sensitization by skin contact
S-Phrases : (26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
(28) After contact with skin, wash immediately with plenty of ...
(36/37/39) Wear suitable protective clothing, gloves and eye/face protection

(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Source : Atofina SA Paris la Défense
22.05.2003

1.6.2 CLASSIFICATION

Classified : provisionally by manufacturer/importer
Class of danger : corrosive
R-Phrases : (26) Very toxic by inhalation
(21/22) Harmful in contact with skin and if swallowed
(34) Causes burns
(43) May cause sensitization by skin contact
Specific limits : no
Source : Atofina SA Paris la Défense
22.05.2003

Classified : provisionally by manufacturer/importer
Class of danger : harmful
R-Phrases : (21/22) Harmful in contact with skin and if swallowed
Specific limits : no
Source : Atofina SA Paris la Défense
22.05.2003

Classified : provisionally by manufacturer/importer
Class of danger : irritating
R-Phrases : (43) May cause sensitization by skin contact
Specific limits : no
Source : Atofina SA Paris la Défense
23.05.2003

Classified : provisionally by manufacturer/importer
Class of danger : very toxic
R-Phrases : (26) Very toxic by inhalation
Specific limits : no
Source : Atofina SA Paris la Défense
22.05.2003

1.6.3 PACKAGING

Memo : TRANSPORT INFORMATION
Source : Atofina SA Paris la Défense
Remark : ADR/RID
N Nr : 3302
Danger No. : 60
Class : 6.1
Packaging group : II
Classification code : T1
Label(s) : 6.1

ADN/ADNR
Material identification No. : 3302
Danger No. : 60
Class : 6.1
Item (letter) : 12°b
Label(s) : 6.1

IMDG
UN Nr (IMDG) : 3302
Class : 6.1
Subsidiary risks: -
Packaging group : II
Label(s) : 6.1
Marine Pollutant (MP) : NO

IATA
N Nr (IATA) or ID Nr : 3302
Class : 6.1
Subsidiary risks: -
Packaging group : II
Label(s) : 6.1

Source : Atofina SA Paris la Défense
22.05.2003 (55)

1.7 USE PATTERN

Type : industrial
Category : Industry Categories: Polymers industry (No.11)
Use Category (IUCLID): Flotation agents (No.23),
ChemUSES Function: Flocculating agents (No.190)
Memo : The polymer products are used for flocculant use in waste water treatment.
The consumption ratio of 2-(dimethylamino)ethyl acrylate and its quarternary ammonium salt for this usage is estimated 95-97% in Japan.
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
04.02.2003

Type : industrial
Category : Industry Categories: Pulp, paper and board industry (No.12)
Use Category (IUCLID): Other (No.0)
ChemUSES Function: Papermaking agents (No.17)
Memo : The polymer products are used for paper industry. The consumption ratio of this substance for this usage is estimated 3-5% in Japan.
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
04.02.2003

Type : type
Category : Non dispersive use
11.02.2000

Type : type
Category : Use in closed system
11.02.2000

Type : industrial
Category : Chemical industry: used in synthesis
11.02.2000

Type : industrial
Category : Polymers industry
11.02.2000

Type : use
Category : Intermediates

11.02.2000

Type : Industrial
Category : Paper, pulp and board industry
Source : Atofina SA Paris la Défense
22.05.2003

MEMO : World-wide and in Japan, 95-97% of this substance is used to produce its quarternary ammonium salts which are used to produce polymers for industries such as water-treatment and paper-making. The remainder is used to produce other copolymers. The use of these polymers is almost exclusively limited to non-dispersive use and exposure to general population is extremely unlikely.
Source : ADAME/HPV Consortium
c/o NIPPON SHOKUBAI CO.,LTD. Osaka
20.03.2003

1.7.1 TECHNOLOGY PRODUCTION/USE

Type : raw material
CAS-No : 79-10-7
EINECS-No : 201-177-9
EINECS-Name : acrylic acid
Remark : esterification process
30.04.2003 : (33)

Type : raw material
CAS-No : 96-33-3
EINECS-No : 202-500-6
EINECS-Name : methyl acrylate
Remark : transesterification process
30.04.2003 : (33)

Type : raw material
CAS-No : 140-88-5
EINECS-No : 205-438-8
EINECS-Name : ethyl acrylate
Remark : transesterification process
30.04.2003 : (33)

Type : raw material
CAS-No : 108-01-0
EINECS-No : 203-542-8
EINECS-Name : 2-dimethylaminoethanol
Remark :
30.04.2003 (33)

Type : Use
CAS-No : 44992-01-0
EINECS-No : 256-176-6
EINECS-Name : [2-(acryloyloxy)ethyl]trimethylammonium chloride
Contents : impurity: acrylic acid < 0.2%
Usage : copolymer for flocculant in order to use in water treatment
Source : Kohjin Co.,Ltd. Tokyo
30.04.2003

Type : Use
CAS-No : 44992-01-0
EINECS-No : 256-176-6

EINECS-Name : [2-(acryloyloxy)ethyl]trimethylammonium chloride
Contents : impurity: 2-(dimethylamino)ethyl acrylate < 0.5%
Usage : copolymer for flocculant in order to use in water treatment
Source : Osaka Organic Chem. Co.,Ltd. Osaka
30.04.2003

Type : Use
CAS-No : 13106-44-0
EINECS-No : 236-029-2
EINECS-Name : [2-(acryloyloxy)ethyl]trimethylammonium methyl sulphate
Source : SNF SA Saint-Etienne
26.05.2003

Type : Use
CAS-No : 46830-22-2
EINECS-No : 256-283-8
EINECS-Name : benzyldimethyl[2-[(1-oxoallyl)oxy]ethyl]ammonium chloride
Source : SNF SA Saint-Etienne
26.05.2003

Type : Use
Generic Name : AROFLOC
Contents : > 90 wt% as solid
Remark : not detected as 2-(dimethylamino)ethyl acrylate
Usage : flocculant in water treatment
Source : Toa Gosei Co.,Ltd. Tokyo
30.04.2003

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : Other
Limit value : VME (TLV-TWA) = 0.5 ppm (2.9 mg/m3)
Short term exposure limit value
Limit value : VLE (TLV-STEL) = 1 ppm (5.8 mg/m3)
Frequency : Times
Remark : These values are set by the ATOFINA Internal Exposure Limits setting Committee.
Source : Atofina SA Paris la Défense
22.05.2003 (18)

Type of limit : MAK (DE)
Limit value :
Remark : Kein MAK-Wert festgelegt.
Source : BASF AG Ludwigshafen
29.09.1994 (58)

1.9 SOURCE OF EXPOSURE

Memo : plant Number
Remark :

Plant Number	Japan	US	EU
Manufacture plant	4	2	3
USE plant	10	11	12

USE includes quats and polymer products
Source : ADAME/HPV Consortium

c/o NIPPON SHOKUBAI CO.,LTD. Osaka

26.05.2003

Memo : Monitored
Remark : Occupational exposure senario: inhalation of mist without breathing protection and dermal of mist without protective wear and gloves in the factory.There are 4 production plants and 10 use plants in Japan, and the atomospheric concentration was messured at one production site [Japan Industrial Safety and Health Association (JISHA), 2000].
Result : The monitored data are shown below.

Operation Data	Monitoring [ppm]	Frequency Time/day	Working Time hr/time
maintenance	1.0-4.4	3	0.055
filling	below detection limit	12	0.5
laying	below detection limit	4	0.5
sampling	below detection limit	10	0.055
analysis	below detection limit	8	0.2

detection limit: 1ppm

Method : Monitoring method;
Air sample was suctioned at the breathing zone of the worker and adsorbed through an absorbent (XAD-2: porous polymer) and desorbed by solvent (butyl acetate) and analyzed by GC.
Remark : Estimated result:
EHEinh = 0.077 mg/kg/day
EHEder = 1.2 mg/kg/day
Calculation formula:
EHEinh = Cair x V x t / W (Observation basis)
EHEder = C x S / W (EASE model basis)

Base data:
Cair = 4.4 [ppm] = 25.7 [mg/m3]
C = 0 - 0.1 mg/cm2/day (EASE model basis)
V = 1.25 [m3/hr]
S = 840 [cm2] (hands surface)
t = 0.055 x 3 = 0.165 [hr/day]
W = 70 [kg]
Comment:
Normally, workers wear protections for eye/face, skin and breathing during the operation work. Hence, the EHEs are considered to substantially lower than the calculationed values.
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
TOAGOSEI CO.,LTD. Tokyo

10.02.2003

Memo : Monitored
Remark : Currently Ciba Speciality Chemicals produces 2-(dimethylamino)ethyl acrylate in two plants world wide (US and UK). Exposure is controlled by engineering solutions. The latest data we have in respect to exposure was taken at the point of manufacture of this substance (UK) and also at the point where it is converted into the quaternary compound (UK).
Result : The highest levels recorded from the exposed workers was found to be 0.02 mg/m3 during the manufacture of this substance and < 0.01 mg/m3 during the conversion to the quaternary compound.
Method : Samples of air were taken over a 6-7 hr period under normal working conditions and the samples analyzed by GC-FID.*
Each worker carries two tubes filled with charcoal.
Air is drawn over the charcoal.
At the end of the shift this substance is extracted using solvent

(Dichloromethane:Methanol 90:10).
Analysis is carried out by GC-FID.

Source : CIBA SPECIALTY CHEMICALS INC. Basel
23.05.2003

Remark : Continuous process.
Transesterification based on ethyl acrylate.
Purification by distillation.
Heavy ends : incineration.
Effluents : biological treatment plant.

Source : Atofina SA Paris la Défense
08.06.1994

Remark : Produced at a single site. The majority is used on-site for chemical synthesis, with some supplied off-site (again for chemical synthesis).

Source : Allied Colloids Ltd. Bradford
05.05.1994

Remark : -Main exposure to workers: at short time working such as cleaning of strainer and sampling
-Process: closed sysytem
-All vent gas: washed and cleaned by alkaline solution
–Heavy ends and waste water: incinerated

Source : NIPPON SHOKUBAI CO.,LTD. Osaka
01.10.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

Type : Handling:
- Engineering controls:
Facilities storing or utilizing 2-(Dimethylamino)ethyl acrylate should be equipped with an eye wash facility and a safety shower. Use process enclosure, local exhaust ventilation, or other engineering controles.
- Personal protective equipment:
Respiratory protection; Chemical cartridge respirator for an organic vapor, or pressure self-contained breathing apparatus.
Eye/face protection; Wear safety glasses with side shields or goggles and a face shield.
Hand, skin and body protection; Wear chemical resistant gloves, a chemical suit, rubber boots.

Source : NIPPON SHOKUBAI CO.,LTD. Osaka
04.02.2003 (37)

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

Memo : UN=3302, Class 6.1
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
17.04.2002 (35)

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : No
No. in directive :
Source : BASF AG Ludwigshafen
29.09.1994 (56)

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

Memo : imupurities of sample; lot no. 5P07 of NIPPON SHOKUBAI CO.,LTD.
Result : contents:
- sample; lot no. 5P07 of NIPPON SHOKUBAI CO.,LTD.

CAS No.	Chemical name	Contents
2439-35-2	2-(dimethylamino)ethyl acrylate	99.9 wt%
108-01-0	2-dimethylamino ethanol	0.01 wt%
79-10-7	acrylic acid	0.01 wt%
150-76-5	methoquinone as inhibitor of polymerization	2000 ppm

Source : NIPPON SHOKUBAI CO.,LTD. Osaka
08.08.2002 (50),(51)

1.16. LAST LITERATURE SEARCH

Type of Search : Internal and External
Date of search
Chapters covered : 1-5
Memo : Document Search were executed by Nippon Shokubai Co.,Ltd in corporation with the cooperative works and database:
Remark : - Exisitng Chemical Inspection Reports:
Japanese MHLW, MOE and CERI
- Database search:
IUCLID (ver.3.1), Beilstein, Toxline, RTECS, MSDS-OHS, MDSD-Aldrich and Chem-Bank

- Toxicological key studies:
Atofina SA
- Indusrial information:
Atofina SA, SNF SA, CIBA Specialty Chem., Toa Gosei, KOHJIN and Osaka Organic Chem.
- Relative chemicals:
IUCLID database and SIDS documents

Source : NIPPON SHOKUBAI CO.,LTD. Osaka
16.05.2003

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : = -80 ° C
Source : Atofina SA Paris la Défense
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.12.2002 (18)

Value : = -92 ° C
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
03.01.2002 (23)

Value : = -75 ° C
Source : NIPPON SHOKUBAI
07.08.2002 (33)

Value : < -60 ° C
Source : Atofina SA Paris la Défense
08.06.1994 (55)

2.2 BOILING POINT

Value : = 172.5 ° C at 1013 hPa
Method : OECD Guide-line 103 "Boiling Point/boiling Range"
Year : 1993
GLP : no
Reliability (1) valid without restriction
Flag Critical study for SIDS endpoint
Source : MITI (Japan)
01.10.2002 (31)

Value : = 167 ° C at
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Value : = 173 ° C at
Source : BASF AG Ludwigshafen
06.04.2002 (23)

Value : = 42 ° C at 1.32 hPa
Decomposition : no
Method : other
GLP : no data
Year : 1976
Source : Allied Colloids Ltd. Bradford
27.05.1994 : (54)

Value : = 59.5 – 61.5 ° C at 14.47 hPa
Decomposition : no
Method : other
GLP : no data
Remark : Handbook data
Source : Allied Colloids Ltd. Bradford
27.05.1994 (35)

Value : = 61.5 – 63.5 ° C at 17.11 hPa
Decomposition : no
Method other
Year : 1972
GLP : no data
Source : Allied Colloids Ltd. Bradford
27.05.1994 (49)

Value : = 75 ° C at 29.3 hPa
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
07.08.2002 (33)

Value : = 90 - 92 ° C at 66.7 hPa
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
07.08.2002 (33)

2.3 DENSITY

Type : density
Value : = 0.94 g/cm3 at 25° C
Method : OECD Guide-line 109 "Density of Liquids and Solids"
Year : 1993
GLP : yes
Test substance :
Source : CERI Report, Japan (Test No.81137K)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.12.2002 (31)

Type : density
Value : = 0.943 g/cm3 at 20° C
Source : Atofina SA Paris la Défense
22.03.2003 (55)

Type : density
Value : = 0.9362 g/cm3 at 20° C
Source : BASF AG Ludwigshafen
05.10.1994 (23)

Type : density
Value : = 0.9406 g/cm3 at 20° C
Method : other
Year : 1972
GLP : no data
Test substance :
Source : Beilstein Online [2001]
03.01.2002 (50)

Type : density
Value : = 0.9434 g/cm3 at 20° C
Method : other
Year : 1949
GLP : no data
Test substance :
Remark : Handbook data.
Source : Beilstein Online [2001]
03.01.2002 (52)

Type : density
Value : = 0.9579 g/cm3 at 20° C
Method : other
Year : 1972
GLP : no data
Test substance :
Source : Beilstein Online [2001]
03.01.2002 (1)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 0.68 hPa at 20° C
Source : Atofina SA Paris la Défense
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.12.2002 (55)

Value : = 1 hPa at 20° C
Source : BASF AG Ludwigshafe
Reliability : (2) valid with restrictions
05.10.1994 (23)

Value : = 24 hPa at 20° C
Decomposition :
Method other (calculated from 0.35 psi)
Year :
GLP :
Test substance :
Source : Sigma-Aldrich Database
Reliability : (3) invalid
07.08.2002 (57)

Value : = 8 hPa at 50° C
Source : BASF AG Ludwigshafen
Reliability : (3) invalid
05.10.1994 (23)

Value : = 13 hPa at 60° C
Source : Atofina SA Paris la Défense
Reliability : (3) invalid
08.06.1994 (55)

2.5 PARTITION COEFFICIENT

Log Kow : = 0.68 at 25° C
Method OECD Guide-line 107 “Partition Coefficient (n-octanol/water), Flask-shaking Method”
Year : 1993
GLP :
Test substance : as prescribed by 1.1 – 1.4
Test condition : 20 rpm during 5 min
pH: 8.5 plus or minus 0.4

Source : MITI (Japan)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.12.2002 (31)

2.6.1 WATER SOLUBILITY

Result : Solubility: 24 g / 100 ml (20 ° C) practically not measurable accurately due to hydrolysis
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
20.01.2003 (49)

Value : at ° C
Qualitative : other
Pka : at 25 ° C
PH : at and ° C
Method :
Year : 1993
GLP :
Test substance : as prescribed by 1.1 - 1.4
Result : The water solubity of 2-(dimethylamino)ethyl acrylate can not be measured, because of influence from it's own hydrolysis.
Source : MITI (Japan)
Reliability : (2) valid with restrictions
04.12.2002 (31)

Value : at ° C
Qualitative : other
Pka : at 25 ° C
PH : = 10.6 at 143 g/L (1 mol/L) and 20 ° C
Method : other
Year : 1999
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : pH value was decreased by hydrolysis

Time after mix. [min]	Temp [° C]	pH
6	20.4	10.6
10	21.6	10.4
20	24.3	10.1
30	26.0	9.5

Result : miscible with hydrolysis
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Test condition : messuerd by pH meter at 5 min after mixing
Reliability : (2) valid with restrictions
20.01.2003 (49)

Value : at ° C
Qualitative : Completely soluble in water
Pka : at 20° C
PH : at and ° C
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Value : at 20 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1991
GLP :
Test substance :
Result : soluble in all proportions with slow hydrolysis
Source : TSCATS 417257 (8EHQ-0291-1119)
07.08.2002 (2)

Value : at ° C
Qualitative : miscible
Pka : at 25 ° C
PH : = 8.5 at and ° C
Source : BASF AG Ludwigshafen
16.11.1994 (23)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 61.7 ° C
Type : closed cup
Method : other
Year : 1999
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : JIS K 2265-96
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Reliability : (2) valid with restrictions
Flag : Material Safety Dataset
04.12.2002

Value : = 62 ° C
Type : closed cup
Method : other: NF M 0.7-019
Year :
GLP : no
Test substance :
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Value : = 67 ° C
Type : open cup
Method : other
Year :
GLP : no
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Value : = 58 ° C
Type :
Method : other: DIN 51 758
Year :

GLP :
Test substance :
Source : BASF AG Ludwigshafen
05.10.1994 (23)

Value : = 66 ° C
Type : closed cup
Method : other
Year :
GLP : no
Test substance : industrial chemical
Remark : measured in-house.
Source : Allied Colloids Ltd. Bradford
27.05.1994

2.8 AUTO FLAMMABILITY

Value : = 209 ° C at 1013 hPa
Method : other
Year :
GLP : no
Source : Atofina SA Paris la Défense
22.05.2003 (55)

Value : = 200 ° C
Method : Other TS: DIN 51 794
Source : BASF AG Ludwigshafen
05.10.1994 (23)

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

Result : 0.6 vol% at 45 ° C in air
5.5 vol% at 88 ° C in air
Source : BASF AG Ludwigshafen
05.10.1994 (23)

Remark : Uncontrolled polymerization could degenerate in explosion.
Source : Atofina SA Paris la Défense
08.06.1994 (55)

Result : explosive under influence of a flame
Method : other
Year :
GLP : no
Test substance : no data
Result : Lowest explosive limit: 1.3% in volume
Source : Atofina SA Paris la Défense
22.05.2003 (55)

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

Memo : Dissociation Exponent (pK)
Result : 7.9 (25 ° C)
Source : Beilstein online (2001)
Test condition : solvent: H2O
method: potentiometric
type : a1/apparent
06.09.2002 (59)

Memo : Dissociation Exponent (pK)
Result : 6.1 (25 ° C)
Source : Beilstein online (2001)
Test condition : solvent: H2O
method: potentiometric
type : b1/apparent
06.04.2002 (59)

Memo : solubility in organic solvents (1)
Result : DMSO: 50 mg/ml
acetone: 50 mg/ml
Source : MWH [Japan]
17.04.2002 (48)

Memo : solubility in organic solvents (2)
Result : 1-octanol; more than 2000 mg/L
acetonitril; more than 1000 mg/L
Source : MITI [Japan]
06.04.2002 (30)

Memo : pH
Result : 8.5 (aqueos solution)
04.04.2002 (38)

Remark : Viscosity: 1.23 mPa.S at 25 ° C
polymerization reaction with radical Intiator and acid
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
05.10.1994 (23)

2.13 VISCOSITY

Test type : Capillary Method
Test procedure :
Value : = 1.29 - mPa s (dynamic) at 20 °C
Result :
Method : other
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Source : Atofina SA Paris la Défense
Reliability : (2) valid with restrictions
22.05.2003

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	= 90.2567 E-12 cm3/(molecule-sec)
Degradation	:	= 50 % after 1.422 hour(s)
Source	:	AOPWIN version 1.90, Syracause Research Co.
Flag	:	Critical study for SIDS endpoint

10.02.2003

3.1.2 STABILITY IN WATER

Type	:	abiotic
Period	:	5 days
Concentration	:	100 mg/L
t1/2 pH4	:	not hydrolyzed at 25 ° C
t1/2 pH7	:	= 12.5 hr at 25 ° C
t1/2 pH9	:	= 1.21 hr at 25 ° C
Deg. Product	:	acrylic acid and 2-dimethylamino ethanol
Method	:	OECD TG 111
Year	:	1997
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The products by hydrolysis were acrylic acid and 2-dimethylamino ethanol which are highly biodegradable.
Source	:	MITI (Japan)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.02.2003 (31)

Type	:	abiotic
t1/2	:	= 0.9 hr, at room temperature and 100 mg/L aqueous solution
Deg. Product	:	acrylic acid and 2-dimethylamino ethanol
Method	:	measurement of the hydrolysis rate to acrylic acid and 2-dimethylamino ethanol by using HPLC and Ion chromatography
Year	:	1993
GLP	:	none
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	equation of hydrolysis: Log C = -0.00556t + 2.01 correlation coeffitient: 0.997 hydrolysis constant: 0.0128 / min
Source	:	MITI (Japan)

14.01.2003 (20)

Type	:	
t1/2	:	= 131.8 min at 25 ° C
Remark	:	rate constant of hydrolysis: k (obs) = 0.00087 1/s
Source	:	BASF AG Ludwigshafen

05.10.1994 (20)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil – water
Method : Calculation according to Mackay, Level III fugacity model
Year : 2002
Method : Distribution were calculated with the following factors

2-(dimethylamino)ethyl acrylate
molecular weight: 143.18
melting point [° C]: -80
vapour pressure [Pa]: 68
water solubility [g/m3]: 240,000
log Kow: 0.68 [25 ° C]
half life [hr] in air: 1.4
in water: 12.5
in soil: 12.5
in sediment: 37.5

Remark : Chemicals Evaluation and Research Institute, Japan (2002):
report on generic fugacity model (Mackay level III)
Result : The potential environmental distribution of 2-(dimethylamino)ethyl acrylate obtained from a generic fugacity model Mackay level III under three emission scenarios is shown as below.

Compartment	Amount % Release 100% to air %	Release 100% to water %	Release 100% to soil %
Air	88.1	0.0	0.0
Water	3.6	100.0	1.1
Soil	8.4	0.0	98.9
Sediment	0.0	0.0	0.0

The results show that if this substance is released into water, it is unlikely to migrate into other compartments. When this substance is released to air, 88.1 % stays in air and 11.9 % is transported into water and soil. In the case of release to soil, it is likely to stay in soil.

Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Reliability : (2) valid with restrictions
20.01.2003 (32)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	predominantly industrial sewage
Contact time	:	related to DOC (Dissolved Organic Carbon)
Degradation	:	= 96 % after 28 day
Result	:	readily biodegradable
Kinetic of test substance	:	7 day = 41 **%** 14 day = 52 **%** 21 day = 96 **%** 28 day = 100 **%** 35 day = 93 **%**
Deg. Product	:	
Method	:	ISO 7827 "Evaluation in an aqueous medium of the 'ultimate' aerobic biodegradability of organic compounds - method by anlaysis of dissolved organic carbon (DOC)"
Year	:	
GLP	:	yes
Test substance	:	other TS: 99.87% purity
Remark	:	Method: OECD 301A and 301E and Directive EEC 84/449 C3 and C4. The latent time t1 (between inoculation and 10% degradation <=7 day and the duration between t1 and 90% of maximum level of degradation was <= 14 day. no inhibitory effect to microorganisms.
Source	:	Atofina SA Paris la Défense
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

05.12.2002 (17)

Type	:	aerobic
Inoculum	:	other: BASF-Belebtschlamm
Concentration	:	related to DOC (Dissolved Organic Carbon)
Contact time	:	
Degradation	:	> 95 % after 28 day
Result	:	
Deg. Product	:	
Method	:	OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year	:	1981
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	CSB = 1025 mg/g BSB30 = 755 mg/g
Source	:	Atofina SA Paris la Défense BASF AG Ludwigshafen

05.10.1994 (19)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : Semistatic
Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 96 hr
Unit : mg/L
Analytical monitoring : Yes
LC50 : n = 8.49
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1997
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4
Result : RESULTS: EXPOSED

- Measured concentrations: in these stock solution (10,000 mg/L) immediately after the preparations

Nominal concentration [mg/L]	Measured concentration [mg/L] 1st preparation (% of nominal)
10,000	8,930 (89)

ND = 10 mg/L

- Effect data (Mortality):

Nominal concentration [mg/L]	Cumulative Mortality (% Mortality) 24 hr	48 hr	72 hr	96 hr
Control	0 (0)	0 (0)	0 (0)	0 (0)
6.00	0 (0)	0 (0)	0 (0)	0 (0)
12.0	4 (40)	10(100)	10(100)	10(100)
24.0	10(100)	10(100)	10(100)	10(100)

24 hr LC50 = 13.1 mg/L (95%c.l. = 6.00 - 24.0 mg/L)
48 hr LC50 = 8.49 mg/L (95%c.l. = 6.00 - 12.0 mg/L)
72 hr LC50 = 8.49 mg/L (95%c.l. = 6.00 - 12.0 mg/L)
96 hr LC50 = 8.49 mg/L (95%c.l. = 6.00 - 12.0 mg/L)
96 hr lowest concentration resulting in 100% mortality = 12.0 mg/L
96 hr highest concentration resulting in 0% mortality = 6.0 mg/L

- Other effects:

Nominal concentration [mg/L]	Symptom of toxicity observed 24 hr	48 hr	72 hr	96 hr
Control	N	N	N	N
Solvent control	N	N	N	N
6.00	N	N	N	N
12.0	AS-1 AQ-1	--	--	--
24.0	--	--	--	--
48.0	--	--	--	--
96.0	--	--	--	--

Note; N : No toxicological symtom was observed
-- : All fish were dead at this observation time

AS : abnormal swimming
AQ : paralyzation
RESULTS: CONTROL
- Nature of adverse effects: none
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Reference substance: $CuSO_4 \cdot 5H_2O$
- Results: 96 hr LC50 = 0.44 mg/L and 0.80 mg/L

Source : MOE Japan (1997a)

Test condition : TEST ORGANISMS
- Strain: *Oryzias latipes*
- Supplier: SANKYO LAB SERVICE CO., LTD. (Japan)
- Size/weight: 19.7 mm (16.8 - 24.1 mm), n = 10 / 0.111 g (0.067 - 0.189 g), n = 10
- Feeding: "TETRAMIN"
- Pretreatment: acclimated for 7 day before testing, mortality was less than 5%. Not fed for 24 hr before the test started.
- Feeding during test: none

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: No solvent was used.

STABILITY OF THE TEST CHEMICAL SOLUTIONS:
2-(dimethylamino)ethyl acrylate is hydrolysed immediately after dilution. T1/2 in 1000 mg/L pure water solution is about 1.5 hr and 99% of this substance disappear after 10 hr.

REFERENCE SUBSTANCE: $CuSO_4 \cdot 5H_2O$

DILUTION WATER
- Source: dechlorinated tap water
- Aeration: aerated sufficiently.
- Alkalinity: 49.0 mg/L
- Hardness: 61.0 mg/L as $CaCO_3$
– Residual chlorine: less than 0.01 mg/L as Cl
- pH: 7.8 (22 ° C)

TEST SYSTEM
- Concentrations: 0, 6.0, 12.0, 24.0, 48.0, 96.0 mg/L
- Renewal of test solution: 24 hr
- Exposure vessel type: size; 5 L test solution in a 5 L glass beaker
- Number of replicates, fish per replicate: 1, 10
- Test temperature: 24±1 ° C
- Dissolved oxygen: 6.3 - 8.3 mg/L
- pH: 7.3 - 8.8
- Intensity of irradiation: not described
- Photoperiod: 16 - 8hr light-dark cycle

DURATION OF THE TEST: 96 hr

TEST PARAMETER: mortality, abnormal behavior, abnormal respiration

SAMPLING: immediately after the preparation

MONITORING OF TEST SUBSTANCE CONCENTRATION: measured by Gas-chromatography

Test substance : SOURCE: Wako Pure Chemical Industries, LTD (Japan)
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: not described
ANY OTHER INFORMATION: Lot No.SKK4558, got on Dec.25,1996

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

20.01.2003 (39)

Type : Semistatic

Species : *Oryzias latipes* (Fish, fresh water)

Exposure period : 14 day

Unit : mg/L

Analytical monitoring : No

NOEC : n = 1.00

LC0 : n = 3.20
LC50 : n = 5.66
Method : OECD Guide-line 204 "Fish, Prolonged Toxicity Test: 14-day Study"
Year : 1997
GLP : Yes
: as prescribed by 1.1 - 1.4
Result : RESULTS: EXPOSED
- Measured concentrations: in these stock solution (10,000 mg/L) immediately after the preparations

Nominal concentration [mg/L]	Measured concentration [mg/L] (% of Nominal) 1st	2nd	3rd
Preparation			
10,000	8,310 (83)	9,960 (100)	8,680 (87)

ND = 10 mg/L

- Effect data (Mortality):

Nominal concentration [mg/L]	Cumulative Mortality (% Mortality) 2 day	4 day	7 day	9 day	11 day	14 day
Control	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1.00	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3.20	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
10.0	7 (70)	10(100)	10(100)	10(100)	10(100)	10(100)

7 d-LC50 = 5.66 mg/L (95%c.l. = 3.20 - 10.0 mg/L)
14 d-LC50 = 5.66 mg/L (95%c.l. = 3.20 - 10.0 mg/L)
14 day lowest test substance concentration resulting in 100% mortality
= 10.0 mg/L
- Other effects:

Nominal concentration [mg/L]	Symptom of toxicity observed 2 day	4 day	7 day	9 day	11 day	14 day
Control	N	N	N	N	N	N
1.00	N	N	N	N	N	N
3.20	AS-1	AS-1	AS-1	AS-1	AS-1	AS-1
10.0	LA AS-1 Fhe-1 Fls-1	--	--	--	--	--

Note; N : No toxicological symtom was observed.
LA : loss of appetite
AS : abnormal swimming
Fhe: fin hemorrhage
Fls : fin loss
-- : All fish were dead at this observation time.

14 day the lowest effective concentration = 3.20 mg/L
RESULTS: CONTROL
- Nature of adverse effects: none
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Reference substance: $CuSO_4 \cdot 5H_2O$
- Results: 96 hr LC50 = 0.44 mg/L

Source : MOE Japan (1997b)

Test condition	:	TEST ORGANISMS - Strain: *Oryzias latipes* - Supplier: SANKYO LAB SERVICE CO.,LTD. (Japan) - Size/weight: 19.6 mm (16.7 - 22.9 mm), n = 10 / 0.132 g (0.072 - 0.218 g), n = 10 - Feeding: "TETRAMIN" - Pretreatment: acclimated for 7 day before testing,mortality was less than 5%. Not fed for 24 hr before the test started. - Feeding during test: 2% of fish weight daily. STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle, solvent: No solvent was used. STABILITY OF THE TEST CHEMICAL SOLUTIONS: 2-(dimethylamino)ethyl acrylate is hydrolysed immediately after dilution. T1/2 in 1000 mg/L pure water solution is about 1.5 hr and 99% of this substance disappear after 10 hr. REFERENCE SUBSTANCE: $CuSO4 \cdot 5H2O$ DILUTION WATER - Source: dechlorinated tap water - Aeration: aerated sufficiently. - Alkalinity: 49.0 mg/L - Hardness: 61.0 mg/L as CaCO3 – Residual chlorine: less than 0.01mg/L as Cl - pH: 7.8 (22 ° C) TEST SYSTEM – Concentrations: 0, 1.0, 3.2, 10.0 mg/L - Dose rate: 3.2 – Renewal of test solution: 1 time per day - Exposure vessel type: size; 5 L test solution in a 5 L glass beaker - Number of replicates, fish per replicate: 1,10 - Test temperature: 24±2 ° C - Dissolved oxygen: 5.2 - 8.4 mg/L - pH: 7.1 - 8.1 - Intensity of irradiation: not described - Photoperiod: 16 - 8 hr light-dark cycle DURATION OF THE TEST: 14 day TEST PARAMETER: mortality, abnormal behavior, abnormal respiration SAMPLING: at 0 day, 4 day and 9 day MONITORING OF TEST SUBSTANCE CONCENTRATION: measured by GC
Test substance	:	SOURCE: Wako Pure Chemical Industries, LTD (Japan) PURITY: 99.9% IMPURITY/ADDITIVE/ETC.: not described ANY OTHER INFORMATION: Lot No.SKK4558, got on Dec.25,1996
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
20.01.2003		(40)

Type	:	Static
Species	:	*Leuciscus idus* (Fish, fresh water)
Exposure period	:	96 hr
Unit	:	mg/L
Analytical monitoring	:	Yes
NOEC	:	= 4.6
LC50	:	= 10 - 22
Method	:	other: DIN 38 412
Year	:	
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Atofina SA Paris la Défense BASF AG Ludwigshafen
Reliability	:	(2) valid with restrictions

Flag : Critical study for SIDS endpoint
02.01.2002 (28)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : Semistatic
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hr
Unit : mg/L
Analytical monitoring : No
NOEC : < 5
EC50 : n = 9.92
EC100 : n = 28
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year : 1997
GLP : Yes
: not specified
Result : RESULTS: EXPOSED
- Nominal/measured concentrations: The concentration was measured immediately after the preparation.

Nominal concentration [mg/L]	Measured concentration [mg/L] 1st preparation (% of nominal)
1000	849 (85%)

- Effect data (Immobilisation):
24 hr EiC50 = 29.5 mg/L (95%c.l. = 25.6 - 33.9 mg/L)
24 hr NOECi =12.0 mg/L
24 hr EiC100 = 65.0 mg/L
48 hr EiC50 = 9.92 mg/L (95%c.l. = 8.43 - 11.5 mg/L)
48 hr NOECi < 5.0 mg/L
48 hr EiC100 = 28.0 mg/L
- Cumulative immobilisation:

Nominal concentration [mg/L]	Cumulative numbers of immobilized Daphnia (% immobility) 24 hr	48 hr
Control	0 (0)	0 (0)
5.00	0 (0)	3 (15)
8.00	0 (0)	4 (20)
12.0	0 (0)	12(65)
18.0	3 (15)	19(95)
28.0	9 (45)	20(100)
42.0	15(75)	20(100)
65.0	20(100)	20(100)
100.0	20(100)	20(100)

RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Reference substance: pure K2Cr2O7
- Results: 48 hr EiC50 = 0.23 mg/L
Source : MOE Japan (1997c)
Test condition : TEST ORGANISMS
- Source/supplier: National Institute for Environmenta Studies

(JAPAN)
- Age: juveniles less than 24 hr old
- Feeding: Chlorella vulgaris, 0.1 - 0.2 mg C / day / individual
- Pretreatment: 2 - 4 week
- Feeding during test: none
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: No solvent was used.
STABILITY OF THE TEST CHEMICAL SOLUTIONS:
2-(dimethylamino)ethyl acrylate is hydrolysed immediately after dilution. T1/2 in 1000 mg/L pure water solution is about 1.5 hr and 99% of this substance disappear after 10 hr.
REFERENCE SUBSTANCE: pure K2Cr2O7
DILUTION WATER
- Source: dechlorinated tap water
- Aeration: aerated sufficiently
- Alkalinity: 52 mg/L
- Hardness: 65 mg/L as CaCO3
– Residual chlorine: less than 0.01 mg/L as Cl
- COD: 1 mg/L
- Ca/Mg ratio: 18 mg/L / 5.3 mg/L = 3.4
- Na/K ratio: 10 mg/L / 1.6 mg/L = 6.3
- pH: 8.2 (22 ° C)
- Conductance: 180 micro S/cm
TEST SYSTEM
- Test type: semistatic
- Concentrations: 0, 5.00, 8.00, 12.0, 18.0, 28.0, 42.0, 65.0, 100 mg/L
- Renewal of test solution: 24 hr
- Exposure vessel type: 100 ml glass beaker
- Number of replicates, individuals per replicate: 4, 5
- Test temperature: 20.0 - 20.1 ° C
- Dissolved oxygen: 8.6 - 8.8 mg/L
- pH: 7.8 - 8.6
- Intensity of irradiation: room light
- Photoperiod: 16 – 8 hr light-dark cycle
DURATION OF THE TEST: 48 hr
TEST PARAMETER: immobility
SAMPLING: immediately after the preparation
MONITORING OF TEST SUBSTANCE CONCENTRATION: measured by Gas-chromatography

Test substance : SOURCE: Wako Pure Chemical Industries, LTD (Japan)
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: not described
ANY OTHER INFORMATION: Lot No.SKK4558, got on Dec.25,1996

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.01.2003 (41)

Type :
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hr
Unit : mg/L
Analytical monitoring : No
NOEC : 10
EC50 : 20 - 28
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year : 1990
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4
Remark : EC50, 24hr = (32 - 43) mg/L
NOEC, 24hr = 18 mg/L
Source : Atofina SA Paris la Défense

Reliability : (3) invalid
05.12.2002 (34)

Type :
Species : other: *Daphnia magna Straus*
Exposure period : 48 hr
Unit : mg/L
Analytical monitoring : No
EC0 : 15.6
EC50 : 24.9
EC100 : 125
Anatical monitoring : no
Method : other: EG-Richtlinie 79/831/EWG, Anhang V, Teil C: Methoden zur Bestimmung der Oekotoxititaet fuer Daphnien-Entwurf-, Stand Mai 1984
Year : 1984
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (3) invalid
Test condition : pH-Wert: 7.9
23.12.2001 (21)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : *Selenastrum capricornutum* (Algae)
Endpoint : biomass
Exposure period : 72 hr
Unit : mg/L
Analytical monitoring : no
NOEC : n = 0.01
EC50 : n = 0.201
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1997
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Result : RESULTS: EXPOSED
- Nominal/measured concentrations: The concentration was measured immediately after the preparation.

Nominal concentration [mg/L]	Measured concentration [mg/L] 1st Preparation (% of nominal)
1000	852 (85%)

ND = 1 mg/L

- Effect data/Element values:
  Area Method
  EbC50 (0-72 hr) = 0.201mg/L (95%c.l.: 0.105 - 0.383 mg/L)
  NOEC (0-72 hr) = 0.010 mg/L
  Rate Method
  ErC50 (24-48 hr) > 1.00 mg/L (95%c.l.: uncalculable)
  NOECr (24-48 hr) = 0.063 mg/L
  ErC50 (24-72 hr) > 1.00 mg/L (95%c.l.: uncalculable)
  NOECr (24-72 hr) = 0.010 mg/L
- Cell density data: average

Nominal concentration [mg/L]	Cell density [x10E+4 cells/ml] 0 hr	24 hr	48 hr	72 hr
control	1.00	4.46	30.7	193.29
0.010	1.00	4.47	28.45	193.69
0.025	1.00	4.12	24.90	144.66
0.063	1.00	3.81	22.96	126.85
0.160	1.00	3.95	22.00	116.69
0.400	1.00	3.46	18.59	79.16
1.00	1.00	2.45	9.61	19.22

- Growth curves:

Nominal concentration [mg/L]	area	Inhibition growth rate (0–72 hr)%	Inhibition growth rate (24-48 hr)%	Inhibition growth rate (24-72 hr)%
0.010		1.6	4.0	0.1
0.025		23.6**	6.5	5.7*
0.063		32.2**	6.9	7.4*
0.160		36.7**	10.7*	10.2**
0.400		54.3**	12.7**	17.1**
1.00		85.2**	30.2**	45.4**

* : Indicates a significant difference (p = 0.05) from the control.
** : Indicates a significant difference (p = 0.01) from the control.

RESULTS: TEST WITH REFERENCE SUBSTANCE:
K2Cr2O7 pure grade
- Results: EbC50 (0 - 72 hr) = 0.41 mg/L

Source : MOE Japan (1997d)

Test condition : TEST ORGANISMS
- Strain: ATCC22662
- Source/supplier: American Type Culture Collection
- Method of cultivation: subculturing in OECD medium until use
- Pretreatment: 3 day
- Initial cell concentration: 1 x 10E+4 cells/ml

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Vehicle, solvent: No solvent was used.
- Other procedures:

STABILITY OF THE TEST CHEMICAL SOLUTIONS:
2-(dimethylamino)ethyl acrylate is hydrolysed immediately after dilution. T1/2 in 1000 mg/L pure water solution is about 1.5 hr and 99% of this substance disappear after 10 hr.
REFERENCE SUBSTANCE: K2Cr2O7 pure grade
GROWTH/TEST MEDIUM CHEMISTRY: OECD medium
TEST SYSTEM
- Test type: static
- Concentrations: 0, 0.010, 0.025, 0.063, 0.160, 0.400, 1.00 mg/L
- Renewal of test solution: none
- Exposure vessel type: 100 ml medium in a 300 ml conical flask, 100rpm shaking
- Number of replicates: 3
- Test temperature: 23.4 - 23.6 ° C
- pH: 7.8 at start and 8.2 - 9.5 at end of the test

Because of consumption CO2, elevation of pH is often encounted in experimental as well as in natural environment.

Nominal concentration [mg/L]	pH 0 hr	72 hr

control	7.8	9.0	
0.010	7.8	9.0	
0.025	7.8	9.5	
0.063	7.8	9.3	
0.160	7.8	9.5	
0.400	7.8	8.8	
1.00	7.8	8.2	

because of consumption CO2, elevation of pH is often encounted in experimental as well as in natural environment

- Intensity of irradiation: 4,000 - 5,000 lux
- Photoperiod: continuous
TEST PARAMETER: cells/ml
MONITORING OF TEST SUBSTANCE CONCENTRATION: gas-chromatography

Test substance : SOURCE: Wako Pure Chemical Industries, LTD (Japan)
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: not described
ANY OTHER INFORMATION: Lot No.SKK4558, got on Dec.25,1996

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
10.12.2002 (42)

Species : *Scenedesmus subspicatus* (Algae)
Endpoint : biomass
Exposure period : 72 hr
Unit : mg/L
Analytical monitoring : no
NOEC : 0.039
LOEC : 0.078
EC10 : 0.08
EC50 : 0.23
EC90 : 0.66
Method : other: EG-Richtlinie 79/831/EWG, Anhang V, C, Algen: Pruefung auf Wachstumshemmung, Mai 1988
Year : 1988
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.10.1994 (20)

Species : *Scenedesmus subspicatus* (Algae)
Endpoint : growth rate
Exposure period : 72 hr
Unit : mg/L
Analytical monitoring : no
EC10 : 0.25
EC50 : 0.88
EC90 : 3.00
Method : other: EG-Richtlinie 79/831/EWG, Anhang V, C, Algen: Pruefung der Wachstumshemmung, Mai 1988
Year : 1988
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
04.10.1994 (20)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : Aquatic
Species : *Pseudomonas putida* (Bacteria)
Exposure period : 17 hr
Unit : mg/L
Analytical monitoring : No
EC10 : 211
EC50 : 444
EC90 : 990
Method : other: Wachstumshemmtest in Anlehnung an Bringmann-Kuehn (DIN 38 412 Teil 8 Entwurf)
Year :
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.10.1994 (22)

Type : Aquatic
Species : other bacteria: BASF-Belebtschlamm
Exposure period : 30 min
Unit : mg/L
Analytical monitoring : No
EC20 : > 1000
Method : other: Bakterientoxizitaet nach Warburg DEV L2
Year : 1977
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Remark : Bis 1000 mg/L kein Hemmeffekt; hoechste gepruefte Konzentration.
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (3) invalid
06.12.2002 (19)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : *Daphnia magna* (Crustacea)
Endpoint : reproduction rate
Exposure period : 21 day
Unit : mg/L
Analytical monitoring : No
NOEC : n = 3.00
LCEC : n = 10.00
EC50 : n = 6.27
LC50 : n = 3.94
Method : OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"

Year : 1997
GLP : Yes
Test substance : not specified
Result : RESULTS: RANGE FINDING TEST: 48hr EiC50 = 9.92 mg/L
RESULTS: EXPOSED
– Nominal/measured concentrations: The concentration was measured immediately after the preparation.

Nominal concentration [mg/L]	Measured concentration [mg/L] (%) Preparation 1st	2nd
1000	826 (83%)	832 (83%)

- Effect data:
21 day LC50 = 3.94 mg/L (95% c.l.: 3.26 - 4.84 mg/L)
21 day ErC50 = 6.27 mg/L (95% c.l.: 0.100 - 10.0 mg/L)
21 day NOECr = 3.00 mg/L
21 day LOECr = 10.0 mg/L

– cumulative reproduction:
(1) Cumulative number of dead parental Daphnia and mortality during exposure of 21day

Nominal concentration [mg/L]	Number of dead parental Daphnia	Mortality (%)	
control	1	(3)	at 20th day
0.100	1	(3)	at 20th day
0.300	2	(5)	at 21th day
1.00	4	(10)	at 21th day
3.00	6	(15)	at 20th day
10.0	40	(100)	at 18th day

(2) mean days required to first brood production during exposure to 2-(dimethylamino)ethyl acrylate:

Nominal concentration [mg/L]	Mean days
control	7.25
0.100	7.00
0.300	7.00
1.00	7.00
3.00	7.00
10.0	7.50

(3) mean cumulative number of juveniles produced per adult during exposure after 21 day

Nominal concentration [mg/L]	Number
control	138.1
0.100	131.8
0.300	80.2
1.00	134.0
3.00	149.4
10.0	13.1

RESULTS: TEST WITH REFERENCE SUBSTANCE
– Results: K2Cr2O7 pure grade: 48 hr EiC50 = 0.23 mg/L (immobility data)
STATISTICAL RESULTS:

Source : MOE Japan (1997e)

Test condition : TEST ORGANISMS
– Supplier: National Institute for Environmental Studies (JAPAN)
- Age: juveniles less than 24 hr old
– Feeding: Chlorella vulgaris, 0.1 - 0.2 mg C / day / individual
– Pretreatment: 2 week
– Feeding during test: Chlorella vulgaris, 0.1 - 0.2 mg C / day / individual
STOCK AND TEST SOLUTION AND THEIR PREPARATION
– Vehicle, solvent: No solvent was used.
STABILITY OF THE TEST CHEMICAL SOLUTIONS:
2-(dimethylamino)ethyl acrylate is hydrolysed immediately after dilution. T1/2 in 1000 mg/L pure water solution is about 1.5 hr and 99% of this substance disappear after 10 hr.
DILUTION WATER
- Source: dechlorinated tap water
– Aeration: aerated sufficiently
– Alkalinity: 52 mg/L
– Hardness: 65 mg/L as CaCO3
– Residual chlorine: less than 0.01 mg/L as Cl
- COD: 1 mg/L
- pH: 8.2 (22 ° C)
– Conductance: 180 micro S/cm
TEST SYSTEM
- Test type:semi-static
– Concentrations: 0, 0.100, 0.300, 1.00, 3.00, 10.0 mg/L
– Renewal of test solution: 2 day
– Exposure vessel type: 800 ml test solution in a 1000 ml glass beaker
– Number of replicates, individuals per replicate: 4, 10
- Test temperature: 19.6 - 20.1 ° C
– Dissolved oxygen: 7.0 - 8.6 mg/L more than 60% of saturated dissolved oxygen concentration
- pH: 7.3 - 8.4
– Intensity of irradiation: room light
– Photoperiod: 16 – 8 hr light-dark cycle
DURATION OF THE TEST: 21 day
ENDPOINTS ASSESSED:
- number of juveniles produced per adult during exposure
- number of dead parental Daphnia magna per day during exposure
SAMPLING: immediately after the preparation on 0 day and 12 day
MONITORING OF TEST SUBSTANCE CONCENTRATION: gas-chromatography

Test substance : SOURCE: Wako Pure Chemical Industries, LTD (Japan)
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: not described
ANY OTHER INFORMATION: Lot No.SKK4558, got on Dec.25,1996

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

10.12.2002 (43)

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Memo : There is no available information specific to 2-dimethylaminoethyl acrylate. Based on the fact that the structurally related compound 2-dimethylaminoethyl methacrylate hydrolyzes in simulated saliva and simulated intestinal fluid to methacrylic acid and dimethylaminoethanol, it can be assumed that this substance hydrolyzes to acrylic acid [CAS No: 79-10-7] and dimethylaminoethanol [CAS No: 108-01-0] in the same circumstances. This is supported by the comparison of acute toxicities between acrylic acid with methacrylic acid and this substance with 2-dimethylaminoethyl methacrylate.

Source : SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]
28.05.2003

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Species : Rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 40
Vehicle : other:paraffin oil
Value : = 455 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1989
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4
Remark : Range of values : 247-1072 mg/kg (95% confidence limit)
Symptoms : Hypocinesia, sedation, piloerection, convulsion
Result : MORTALITY:
Cumulated Mortality

Sex	Dose [mg/kg]	day 1	day 2	day 5	day 6	day 15	% of mortality
Male	80	0	0	0	0	0	0
	160	0	0	0	0	0	0
	320	0	0	0	1	1	20
	640	4	4	4	4	4	80
	2000	5	5	5	5	5	100
Female	160	0	0	0	0	0	0
	320	2	3	3	3	3	60
	2000	5	5	5	5	5	100

CLINICAL SIGNS: Hypocinesia, sedation, piloerection dyspnea, toxicoclonic convulsions followed by death, lateral recumbency, mortality. These signs appeared within minutes of treatment and persisted for four hours to six days in surviving animals, depending on dosages administered.
NECROPSY FINDINGS: No abnormality observed in animals sacrificed at the end of the study. In the animals found dead during the study; the glandular section of the stomach and the intestines appeared abnormally reddish in two females at 320 mg/kg, in 4 males at 640 mg/kg, and in all animals at 2000 mg/kg.
SEX-SPECIFIC DIFFERENCES: No sex-related differences in toxicity were noted.

Source : Atofina SA Paris la Défense

Test condition : ADMINISTRATION:
- Doses: 80, 160, 320, 640 and 2000 mg/kg, 5 animals/sex/group
- Volume administered: a constant volume of 10 ml/kg at each dosage

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.12.2002 (7)

Type : LD50
Species : Rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 5
Vehicle : CMC
Value : = 1200 - 1500 mg/kg bw
Method : other: BASF Test
Year : 1978
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Result : MORTALITY:
- Time of death:

Sex	Dose [mg/kg]	1 hr	1 day	2 day	7 day	14 day
Male	1000	0	0	0	0	0
	1210	0	0	0	0	0
	1470	3	5	5	5	5
	2150	4	5	5	5	5
	3160	5	5	5	5	5
	5000	5	5	5	5	5
Female	1000	0	0	0	0	0
	1210	0	0	0	0	0
	1470	2	5	5	5	5
	2150	5	5	5	5	5
	3160	5	5	5	5	5

- Number of deaths at each dose:

Dose [mg/kg]	Dead animals after 14 day	Moltality(%)
1000	0	0
1210	0	0
1470	10	100
2150	10	100
3160	10	100
5000	10	100

CLINICAL SIGNS:
NECROPSY FINDINGS:
POTENTIAL TARGET ORGANS:
SEX-SPECIFIC DIFFERENCES: none

Source : BASF AG Ludwigshafen
Test condition : ADMINISTRATION:
- Volume administered or concentration: 10 ml/kg
- Post dose observation period: 14 day

EXAMINATIONS:
Test substance : Reinheit: > 90 %
Reliability : (3) invalid
10.12.2002 (26)

Type : LD50

Value	:	> 200 mg/kg bw
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	60
Vehicle	:	other
Doses	:	25, 200, 2000, 5000 mg/kg
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1985
GLP	:	yes
Test substance	:	As prescribed by 1.1 - 1.4
Test condition	:	vehicle= arachid oil
Remark	:	Range of value > 200 and 2000 mg/kg This value is consistent with an LD50 in rat per as according EPA obtained by Elf Atochem) 455 mg/kg. Symptoms were hunched posture, piloerection, lethargy, ptosis, ataxia and Bradypnea.
Source	:	ATOFINA SA Paris la defense

10.12.2002 (5)

Type	:	LD50
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	215 - 681 mg/kg bw
Method	:	other: BASF Test
Year	:	
GLP	:	No
Test substance	:	As prescribed by 1.1 - 1.4
Source	:	BASF AG Ludwigshafen
Reliability	:	(3) invalid

29.09.1994 (29)

Type	:	LD50
Species	:	Rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 533 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1989
GLP	:	yes
Test substance	:	As prescribed by 1.1 - 1.4
Source	:	Allied Colloids Ltd. Bradford
Reliability	:	(3) invalid

04.05.1994

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	40
Vehicle	:	No data
Exposure time	:	4 hr

Value : = 0.066 mg/L
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year : 1991
GLP : yes
Test substance : As prescribed by 1.1 - 1.4
Remark : Vapor + Aerosol. Symptoms : Gasping, lethargy, noisy respiration.
Result : MORTALITY:
- Time of death:
In group 0.0058 mg/L, one male died overnight following exposure.
In group 0.037 mg/L, two males died on day 1 (pm) of the observation period.
In group 0.092 mg/L, two male and two females died overnight following exposure. One male died on day 1(pm). One male and two females were found dead on day 2 (am) and one female died on day 2 (pm) of the observation period.
In group 0.460 mg/L, one male rat and one female rat died during exposure. Two male rats and two female rats died within 2 hr post exposure. One male rat died avernight following exposure. One male rat and two female rats werefound dead on day 2 (am) of the observation period.

- Number of deaths at each dose:

Level [mg/L]	Mortality Males	Females	Total
Control	0/5	0/5	0/10
0.037	2/5	0/5	2/10
0.058	1/5	0/5	1/10
0.092	4/5	5/5	9/10
0.460	5/5	5/5	10/10

CLINICAL SIGNS:
- (a) During exposure:
The signs seen during exposure were considered to be consistent with inhalation of an irritant aerosol included partial closing of of the eyes exaggerated respiratory movements irregular respiration rate, adoption of a hunched body posture and gasping. One male and one female exposed at 0.460 mg/L died during exposure.
- (b) During obsevation period:
At the time of removing of the rats from exposure chamber (day 0), gasping, wet fur and lethargy was observed.
On day 1 and later, were noisy respiration, rales and brown staining.
No death was recorded after day 2.
Recovery was observed from day 4 and all surviving animals were normal in appearance and behaviour by day 7 of the observation period.
- c) Bodyweight:
Moderate to marked decreases of bodyweight or reducion in the rate of bodyweight gain for up to 3 day following exposure.
Weight gain for rats that survived was similar to that of the controls.
– NECROPSY
The lung weight to bodyweight ratio was increased, due to high lung weight in rat that died folowing exposure to 2-(dimethylamino)ethyl acrylate. The ratios were within normal limits for rats that survived.

Lung weight to body ratios (male)

Group (mg/L)	Rat	Lung weight (g)	Body-weight (g)	Lung to bodyweight ratio (LW X 100BW)

				Survivors	Decedents	
Control	1	1.44	314	0.46	----	
	2	1.36	343	0.40	----	
	3	1.49	338	0.44	----	
	4	1.17	293	0.40	----	
	5	1.35	321	0.42	----	
Mean				0.42		
SD				0.026		
0.460	11	1.35	214	----	0.63	
	12	2.43	179	----	1.36	
	13	1.25	205	----	0.61	
	14	1.37	223	----	0.61	
	15	2.40	212	----	1.13	
Mean				0.87		
SD				0.354		
0.092	21	1.89	173	----	1.09	
	22	1.43	279	0.51	-----	
	23	2.42	199	----	1.22	
	24	1.39	169	----	0.82	
	25	1.50	203	----	0.74	
Mean				0.97		
SD				0.225		
0.037	31	1.37	287	0.48	-----	
	32	1.51	334	0.45	-----	
	33	1.87	191	----	0.98	
	34	2.46	195	----	1.26	
	35	1.37	326	0.42	----	
Mean				0.45	1.12	
SD				0.030	----	
0.058	41	1.72	312	0.55	----	
	42	1.77	317	0.56	----	
	43	1.56	328	0.48	----	
	44	1.59	287	0.55	----	
	45	1.35	213	----	0.63	
Mean				0.54		
SD				0.037		

Lung weight to body ratios (female)

Group	Rat	Lung weight (mg/L)	Body-weight (g)	Lung to bodyweight ratio (LW X 100BW) (g)		
				Survivors	Decedents	
Control	6	1.36	265	0.51	----	
	7	1.23	268	0.46	----	
	8	1.27	252	0.50	----	
	9	1.37	260	0.53	----	
	10	1.17	269	0.43	----	
Mean				0.49		
SD				0.040		
0.460	16	1.41	223	----	0.63	
	17	1.75	211	----	0.83	
	18	2.13	176	----	1.21	

	19	2.99	193	----	1.55
	20	1.77	209	----	0.85
Mean			1.01		
SD			0.365		
0.092	26	1.59	166	----	0.96
	27	1.98	207	----	0.96
	28	2.26	186	----	1.22
	29	2.35	218	----	1.08
	30	2.09	181	----	1.15
Mean			1.07		
SD			0.115		
0.037	36	1.23	257	0.48	-----
	37	1.24	238	0.52	-----
	38	1.34	256	0.52	-----
	39	1.41	280	0.50	-----
	40	1.31	239	0.55	----
Mean			0.51		
SD			0.026		
0.058	46	1.34	244	0.55	----
	47	1.36	258	0.53	----
	48	1.33	244	0.55	----
	49	1.49	251	0.59	----
	50	1.36	243	0.56	----
Mean			0.56		
SD			0.022		

NECROPSY FINDINGS:
- Macroscopic findind;
The findings for rats that died as a result of exposure were typified by congestion, and a swollen appearance of the lungs. The stomach of a number of decedents were gas-filled.
There were no treatment-related macroscopic abnormalities in rats that survived exposure to this substance.
- Microscopic observation;
Lungs: Minimal vascular congestion and areas of pulmonary edema in many of the decedents rats.

Source : ATOFINA SA Paris

Test condition : TEST ORGANISMS:
- Source: Charles Rivers UK
- Age: 6 week old males and 8 week old females
- Weight at study initiation: ca. 200 g
- Number of animals: 40, 5 males and 5 females / group
- Controls: 10

ADMINISTRATION:
- Type of exposure: whole body exposure in exposure chamber containing a liquid droplet aerosol generated from this substance.
- Concentrations: 0.037, 0.058, 0.092 and 0460 mg/L
- Duration of exposure: 4 hr
- Observation period: 14 day post exposure
– Concentrations:

ADAME in air [mg/L]	Variation (%)
0.058	5
0.037	32
0.092	35

		0.460 67
		ADAME = 2-(dimethylamino)ethyl acrylate
		Variation = range x 100 / mean
		- Particle size: Approximately 82% to 90% of this substance present in the chamber atmosphere was in the form of or associated with particles of respirable size (< 5.5 um aerodynamic diameter).
		- Type of preparation of aerosol The aerosol generator was designed to produce and maintain an atomosphere containing a high propotion of respirable droplets. All parts of the generator in contact with this substance were made of stainless steel or glass. This substance was supplied to the generator from a syringe driven at a constant rate by a syringe pump. The compressed air supply to the generator was dried, filtered and oil-free.
Result	:	The LC50 (4 hr) for 2-(dimethylamino)ethyl acrylate is estimated as 0.066 mg/L of air. The standard error of the estimate is 0.007 mg/L.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
20.12.2002		(9)
Type	:	LC50
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	30
Vehicle	:	
Exposure time	:	1 hr
Value	:	= 0.972 mg/L
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The gravimetric deterninations of concentration and particle size distribution are indicative only of the solid phase or non evaporated liquid phase of the test article. Any vapor component or any fraction which might evaporate or sublimate is not accounted for.
Result	:	MORTALITY:
		- Time of death: No female died during and after exposure. In group 2, one male died on the test day 2 and one on test day 3. One male of group 3 died shortly after exposure, two others on test day 2, and one on test day 3.

- Mortality at each dose:

Groups	1	2	3
Concentration [g/L air]	0.512	0.895	1.237
Males (%)	0	40	80
Females (%)	0	0	0
Both Sexes (%)	0	20	40

CLINICAL SIGNS:
- Group 1 (0.512 mg/L): Restlessness was noted in one male during exposure. Hunched posture, labored respiration and rales were observed in both sexes following exposure. None of these signs persisted more than 5 day.
- Group 2 (0.895 mg/L): Rsstlessness and labored respiration were noted in a few animals during exposure. A number of signs were noted in both sexes following exposure: sedation, hunched posture, laboured

respration, rales, stiff gait; in the males: ventral recumbency, and in the females: excitement, serious rhinorrhea, chromodacryorrhea and lid adhesion. Breathing diffiiculties and hunched posture lasted 6-7 day, whereas other signs disappeared after 2-3 day.
- Group 3 (1.237 mg/L): Restlessness, labored respiration (both sexes) as well as salivation and serous rhinorrhea (females) were noted in a few animals during exposure. Except for chromodacryorrhea and lid adhesion, the signs observed in group 2 as well as ruffled fur were also noted in group 3. Hunched posture and breathing difficulties disappeared after test-day 8.

NECROPSY FINDINGS:
- Macroscopic Observations
There were no definite treatment-related necroscopy findings identified as the majority of changes were considered to be due to post-mortem congestion in the premature decedants.
- Microscopic Observations
Necrosis and exudation was seen in the nasal cavities (levels 1+2), larynx and trachea of all premature decandants, with the exudate being purulent in animals which survived the treatment period.
some animals of group 2 (0.895 mg/L air) and 3 (1.237 mg/L air) which survived the observation period showed epithelial hyperplasia, sometimes with keratinisation in the larynx, but the degree of recovery was high.
No pathological evidence of toxicity was seen in group 1 animals (0.512 mg/L air).

SEX-SPECFIC DIFFERENCES: No death was recorded in the females.

Source : Atofina SA Paris la Défense

Test condition : TEST ORGANISMS:
- Source: BRL ltd, CH-4414 Fuelleinsdorf / Switzerland
– Ages: males; 10 week, females; 12 week
- Weight at study initiation: males; 182.4 - 200 g, females; 180.8 - 198.8 g
- Number of animals: 15 males, 15 females
- Controls: no

ADMINISTRATION:
- Type of exposure: whole body
– Concentrations etc.:

Groups	1	2	3
Nominal concentration [mg/L air]	0.568	0.890	1.386
Analytical concentration [mg/L air]	0.512	0.895	1.237
Gravimetric*	0.0001	0.0002	0.0004
Temperature [° C]	23.1(a)	23.0(a)	24.0(a)
	23.9(b)	24.2(b)	24.2(b)
Relative Humidity [% rh]*	0.3(a)	1.0(a)	1.1(a)
	57.8(b)	42.2(b)	50.5(b)

(a): At the entry of the exposure chamber
(b): At the exit of the exposure chamber
* : The compressed air supply was specially filtered with silica gel to reduce the relative humidity.

- The oxygen concentration in the exposure chamber:
At the entry of the exposure chamber: 20.9 vol%
At the exit of the exposure chamber: 20.5 - 20.6 vol%
- Particle size: The parcentage of particles found on the 3 um or less stage of the impactor was 100% in all groups.

Result : The LC50 of 2-(dimethylamino)ethyl acrylate for this 1 hr acute inhalation toxicity study in rats of both sexes observed over a period of 15 day was estimated to be:

Animals	Males	Females	Both Sexes
LC50 [mg/L air]	0.972	> 1.237	1.342
95% confidence limit	0.924-1.022	-	1.199-1.503

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.12.2002 (11)

Type : LC100
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 4 hr
Value : < 0.352 mg/L
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year :
GLP : yes
Test substance : As prescribed by 1.1 - 1.4
Remark : 10/10 + (Vapor only). Symptoms : Restlessness ; Labored respiration ; Dyspnea ; sedation.
Source : Atofina SA Paris la Défense
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
16.11.1994 (10)

Type : LC50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 4 hr
Value : 0.22 mg/L
Method : other: BASF Test
Year :
GLP : no
Test substance : As prescribed by 1.1 - 1.4
Remark : Dampf-Exposition
Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
Test condition : Reinheit: > 90 %
29.09.1994 (27)

Type : other: IRT
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time :
Method : other: BASF Test
Year :
GLP : no
Test substance : As prescribed by 1.1 - 1.4
Remark : Nach 10-minuetiger Exposition in einer bei 20 Grad Celsius mit der Substanz angereicherten Atmosphaere starb keines der

12 in den Versuch eingesetzten Tiere. Todesfaelle traten nach laengerer Exposition auf.

Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
Test condition : Reinheit: > 90 %
29.09.1994 (26)

Type : LC50
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 4 hr
Value : > 0.06 mg/L
Method : OECD Guide-line 403 "Acute Inhalation Toxicity"
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : Vapor only. 2/10 + Abnormal respiration.
Source : Atofina SA Paris la Défense
16.11.1994 (13)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Species : rat
Strain : Spraque-Dawley
Sex : male/female
Number of animals : 60
Vehicle : Other: paraffin oil
Value : = 419 mg/kg bw
Method : OECD Guide-line 402 "Acute dermal Toxicity"
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : Range of values : 253-593 mg/kg.
Symptoms : Sedation ; Piloerection ; Hypocinesie – tremors ; skin irritation.

Result : MORTALITY:
- Time of death:
Mortality was noted principally with in the 24 hr following tratment, and on day 7 in one animal at the dose level of 330 mg/kg.

- Numbers of deaths and Cumulated Mortality

Sex	Dose [mg/kg]	Volume [ml/kg]	day 1	day 2	day 5	day 7	15	% of Mortality
Male	200	5	0	0	0	0	0	0
	330	5	0	2	2	3	3	60
	500	5	0	3	3	3	3	60
	700	5	1	3	3	3	3	60
	980	5	3	5	5	5	5	100
	1400	5	5	5	5	5	5	100
	2000	5	0	5	5	5	5	100

	2000	2.12	0	5	5	5	5	100
Female	700	5	0	2	2	2	2	40
	980	5	3	5	5	5	5	100
	2000	5	0	5	5	5	5	100
	2000	2.12	0	5	5	5	5	100

- Mortality at each dose
Male & Females:

Dose [mg/kg]	200	330	500	700	980	1400	2000
Mortality (%)	0	60	60	60	100	100	100

CLINICAL SIGNS:
4 to 6 hr after application of 2-(dimethylamino)ethyl acrylate, a moderate to severe decrease in spontaneous activity was observed in all animals at all doses. The general behaviour of the surviving animals was normal on day 3, in all animals treated at 200 and 500 mg/kg, in 2/3 at animals at 330 mg/kg, and in 4/5 animals at 700 mg/kg. The symptoms persisted in 1 animal at 330 mg/kg until death on day 7 and in 1 animal at 700 mg/kg until day 15. Clearly visible cutaneous reactions (erythema, dryness, desquamation) were observed after 4 day in the surviving animals treated at 700 mg/kg.
NECROPSY FINDINGS:
The macroscopic examination of the main organs of the animals found dead during the study or sacrificed at the end of the observation period revealed not apparent abnormalities at dose levels; 200, 500, 980, 1400, and 2000 mg/kg.
SEX-SPECIFIC DIFFERENCES: No sex related toxicity was observed.

Source : Atofina SA Paris la Défense
Test condition : TEST ORGANISMS:
- Source: IFFA CREDO, BP 109 69210 L'ARBRESLE , France
- Age: 8 week
- Weight at study initiation: 274 +/-11 g for the males,
211 +/- 9 g for the females

ADMINISTRATION:
- Area covered: 5 x 7 cm
- Occlusion: The animals were wrapped with a semi-occlusive dressing for 24 hr.
- Vehicle: paraffin oil
- Total volume applied: 5 ml/kg and 2.12 for one dose level 2000 mg/kg
- Removal of test substance: no rinsing off of the skin

EXAMINATIONS: no histological examination
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.12.2002 (8)

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : = 891 mg/kg bw
Method : OECD Guide-line 402 "Acute dermal Toxicity"
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Source : Allied Colloids Ltd. Bradford
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

04.05.1994

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : 50 - 200 mg/kg bw
Method : other: BASF Test
Year :
GLP : no
Test substance : not specified
Source : BASF AG Ludwigshafen
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
Test substance : Reinheit: > 90 %
30.11.2002 (26)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Species : mouse
Strain : NMRI
Sex : male/female
Number of animals : 5
Vehicle : CMC
Route of admin. : i.p.
Exposure time :
Value : ca. 200 mg/kg bw
Method : other: BASF Test
Year : 1978
GLP : no
Test substance : not specified
Result : MORTALITY:
- Time of death:

Sex	1 hr	1 day	2 day	7 day	14 day	
Male		0	0	1	2	2
Female		0	0	1	3	3

CLINICAL SIGNS:
NECROPSY FINDINGS:
POTENTIAL TARGET ORGANS:
SEX-SPECIFIC DIFFERENCES: none
Source : BASF AG Ludwigshafen
Test condition : ADMINISTRATION:
- Volume administered or concentration: 10 ml/kg, 2 w/v %
- Post dose observation period: 14 day
EXAMINATIONS:
Test substance : Reinheit: > 90 %
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.12.2002 (26)

Type : LD50
Species : rat

Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Route of admin.	:	i.p.
Exposure time	:	
Value	:	= 183 mg/kg bw
Method	:	
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Range of values : 146-229 mg/kg. Symptoms : Depression of motor activity and periodic seizures.
Source	:	Atofina SA Paris la Défense
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

09.05.1994 (54)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	4 hr
Number of animals	:	6
Vehicle	:	No data
PDII	:	8
Result	:	corrosive
EC classification	:	corrosive (causes burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1984
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The cutaneous reactions were observed 1, 24, 48, 72 hr and 7 day after removal of the patch.
Result	:	

Exposure	1 hr		4 hr	
Method	S.O.	O	S.O.	O
Results	C	C	C	C

S.O.; Semi-occlusive
O ; Occlusive
C ; Corrosive

Source	:	Atofina SA Paris la Défense
Test condition	:	TEST ANIMALS: - Source: New-Zealand Rabbits - Weight at study initiation: 2 - 4 kg - Number of animals: 6 ADMINISTRATION/EXPOSURE - Occlusion: 0.5 ml/patch were applied to gauze pads 3 cm x 3 cm. The patches were fixed on the prepared skin areas of the flanks and covered by wrapping an air-permeable circular bandage (semi-occlusive method) or air-tight plastic foil (occlusive method) around animals.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

10.12.2002 (51)

Species : rabbit
Concentration :
Exposure :
Exposure time : 72 hr
Number of animals : 3
PDII : 7.6
Result : corrosive
EC classification : corrosive (causes burns)
Method : Draize Test
Year : 1979
GLP : no
Test substance : not specified
Method : Feedral Register 38, No.187,1500.41, S.27029 (27.09.1973)
Result :

Animal	Effects	Method	Observation Interval 24 hr	72 hr	8 day
No.1	Erythema	not abraded	4	4	E
		abraded	4	4	E
	Oedema	not abraded	4	3	E
		abraded	4	3	E
No.2	Erythema	not abraded	4	4	4
		abraded	4	4	4
	Oedema	not abraded	4	4	2
		abraded	4	4	2
No.3	Erythema	not abraded	2	4	4
		abraded	4	4	4
	Oedema	not abraded	3	4	3
		abraded	4	4	3

E = Eiterung

Source : BASF AG Ludwigshafen
Test substance : Reinheit: > 90 %
Result : Primary Irritation Index:
= (Sum Erythema 24/72 hr + Sum Oedema 24/72 hr) / 4 x no of animals
= 91/12 = 7.6
Reliability : (2) valid with restrictions
Flag : Critical study SIDS endpoint
20.01.2003 (26)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 72 hr
Number of animals : 6
PDII : 8
Result : corrosive
EC classification : corrosive (causes burns)
Method : Draize Test
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : The recommendations of the Federal Hazardous Substances Labelling Act
Regulations, Section 191.11, published in the Federal Register (USA) 29 F.R. 13009, 1964
Remark : The cutaneous reactions were observed when the patches were removed and were again made at 72 hr.
Result : 0.5 ml as such was applied under occluded patch for 24 hr on abraded

and
intact skin. Primary irritation score of 8 (maximum) was obtained, likely due to the rapid hydrolysis.
Severe erythema, turgor, discolouration, tissue destruction and blackening
characterized the reactions exhibited 24 and 48 hr following application.

Source : Atofina SA Paris la Défense

Test condition : TEST ANIMALS:
- Strain: New Zealand white Rabbits
- Weight at study initiation: 2-2.5 kg
- Number of animals: 6
- Controls: 0

ADMINISTRATION/EXPOSURE
- Preparation of test substance: undiluted
- Area of exposure: 1 inch x 1 inch
- Occlusion: surgical gauze patches secured by impervious adhesive tape
  and further occluded with a "Stockinette" sleeve covering the entire trunk
  of the animals
- Vehicle: none
- Total volume applied: 0.5 ml
- Postexposure period: 48 hr
- Removal of test substance: no

Reliability : (2) valid with restrictions

Flag : Critical study SIDS endpoint

10.12.2002 (3)

5.2.2 EYE IRRITATION

Species : rabbit

Concentration : undiluted

Dose : 0.1 ml

Exposure Time : 0.07 min

Comment : rinsed after (see exposure time)

Number of animals : 2

Result : corrosive

EC classification : risk of serious damage to eyes

Method : other

Year : 1981

GLP : no

Test substance : as prescribed by 1.1 – 1.4

Method : Modified Draize test from that laid down in the Federal Hazardous Substances Labelling Act Regulations, Section 191.12, published in the Federal Register (USA) 29 F.R. 13009, 1964

Remark : The lids were gently held together for one second then the eye was rinsed with 20 ml lukewarm water 4 sec after instillation.

Result : Marked cornceal, iris and conjunctival lesions were displayed by both animal within 1 hr of instillation.

Source : Atofina SA Paris la Défense

Test condition : TEST ANIMALS:
- Strain: New Zealand white Rabbits
- sex: females
- Weight at study initiation: 2 - 2.5 kg
- Number of animals: 2
- Controls: 0

ADMINISTRATION/EXPOSURE
- Preparation of test substance: undiluted

- Area of exposure: one eye per animal
- Vehicle: none
- Total volume applied: 0.1 ml
- Postexposure period: 1 hr
- Removal of test substance: rinsed with lukewarm distilled water.

The animals were sacrificied 1 hr after the instillation.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.12.2002 (4)

Species : rabbit
Concentration :
Dose :
Exposure Time : 72 hr
Comment :
Number of animals : 3
Result : corrosive
EC classification : risk of serious damage to eyes
Method : Draize Test
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 – 1.4
Method : Feedral Register 38, No.187,1500.41, S.27019 (27.09.1973)
Result :

Animal No.1:			day 1	day 2	day 3	day 8
1. Cornea	Opacity	(a)	1	*	*	3
	Area involved	(b)	4	*	*	4
	(a) x (b) x 5 (Max. 80)		20	-	-	
2. Iris		(c)	0	*	*	1
	(c) x 5 (Max.10)		0	-	-	
3. Conjucctive	Redness	(d)	2	2	*	2
	Chemosis	(e)	4	4	4	2
	Dicharge	(f)	3	3	3	3
	((d)+(e)+(f)) x 2 (Max.20)		16	18	14	
4. Subtotal	=1.+ 2.+ 3. (Max.110)		36	18	14	
Animal No.2:						
1. Cornea	Opacity	(a)	2	*	*	3
	Area involved	(b)	4	*	*	4
	(a) x (b) x 5 (Max.80)		40	-	-	
2. Iris		(c)	*	*	*	*
	(c) x 5 (Max.10)		-	-	-	
3. Conjucctiva	Redness	(d)	2	2	*	2
	Chemosis	(e)	4	4	4	3
	Discharge	(f)	2	3	3	3
	((d)+(e)+(f)) x 2 (Max.20)		16	18	14	
4. Subtotal	=1.+ 2.+ 3. (Max.110)		56	18	14	
Animal No.3:						
1. Coenea	Opacity	(a)	2	2	*	3
	Area involved	(b)	4	4	*	4
	(a) x (b) x 5		40	40	-	

	(Max.80)					
2. Iris		(c)	*	1	*	1
	(c) x 5		-	5	-	
	(Max.10)					
3. Conjuctiva	Redness	(d)	2	2	*	2
	Chemosis	(e)	4	3	4	3
	Discharge	(f)	2	2	3	
	((d)+(e)+(f)) x 2		16	14	14	
	(Max.20)					
4. Subtotal	=1.+ 2.+ 3.		56	59	14	
	(Max.110)					

Modified Maximum Average Score:
(36 + 56 + 56) / 3 = 49 at 1st test day.

Source : Atofina SA Paris la Défense
BASF AG Ludwigshafen
Test substance : Reinheit: > 90 %
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
20.01.2003 (26)

5.3 SENSITIZATION

Type : Freund's complete adjuvant test
Species : guinea pig
Number of animals : 30
Vehicle : other
Result : sensitizing
Classification : sensitizing
Method : OECD Guid-line 406 “Skin Sensitization“
Year : 1989
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : A modified Magnusson and kligman method
Remark : Type : Guinea pig maximization test.
Concentration used :
Intradermal ; 0.5 % in paraffin oil, day 1
Topical ; 5 % in paraffin oil on day 9-10
Challenge ; 5% in paraffin oil on day 26
Result : RESULTS OF TEST : 100 % of 10 male + 10 female positive
- Sensitization reaction: on day 11, after removal of the dressing, no cutaneous reactions were noted in the control animals. At the intradermal injection sites, marked cutaneous lesions (chaps) were noted in the treated animals.
- Afer the challenge:
24 hr after the removal of patches: very slight (score 1) erythema was observed in 3/9 males and 4/10 females. A well defined (2) erythema was observed in 6/9 males and 6/10 females.
48 hr after the removal of patches: very slight (score 1) erythema was observed in 3/9 males and 5/10 females. A well defined (2) erythema was observed in 6/9 males and 5/10 females.
- Clinical signs: One male of the treated group was found dead on day 9 having showed no clinical signs in the preceeding day. At the animal examination, traces of a red liquid were seen in the nose.
MICROSCOPIC EXAMINATION:
Due to some "doubtful" macroscopic reactions, an histological examination was performed on the cutaneous samples of all treated animals.
At the treated site:

- moderate hyperkeratosis in 9/9 males and moderate to marked in 10/10 females.
- moderate acanthosis in 9/9 males and moderate to marked in 10/10 females.
- moderate to marked mononucleated cell infiltration in 9/9 males and 10/10 females
- slight to moderate vascular ectasia in 2/9 males and moderate in 1/10 female.

At the non treated site; No abnormalities were observed.

Source : Atofina SA Paris la Défense

Teat condition : TEST ANIMALS:
- Strain: Dunking Hartley
- Sex: males and females
- Source: Shamroch Bio Service Breeding Center ,78150 Gambais, France
- Weight at study initiation: 336 +/- 11 g for the males, 327 +/- 10 g for the females
- Number of animals: 10/sex
- Controls: 5/sex

ADMINISTRATION/EXPOSURE
- Study type: Guinea Pig Maximisation Test from Magnusson and Kligman
- Preparation of test substance for induction:
  Type Intradermal in Freuds Complete Adjuvant (FCA): 0.5% in paraffin oil on day 1
  Type topical: 5 % in paraffin oil on day 9-10
  Challenge : 5% in paraffin oil on day 26
- Positive control: no

EXAMINATIONS scoring of erythema and for oedema formation
- Grading system: scoring scale 0 to 4

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

20.12.2002 (6)

5.4 REPEATED DOSE TOXICITY

Type	:	OECD combined study TG 422, combined repeat dose and reproductive/developmental (one generation) toxicity screening test
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	males; 43 day females; from 14 day before mating to day 3 of lactation
Frequency of treatment	:	once daily
Post obs. period	:	1 day
Doses	:	0 (vehicle), 4, 20, 100 mg/kg/day
Control group	:	yes, corn oil
NOAEL	:	= 20 mg/kg bw
Method	:	OECD combined repeat dose and reproductive/developmental toxicity screening test
Year	:	1997
GLP	:	yes
Test substance	:	other TS: 99.9 wt% purity, NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
Remark	:	As the LD50 value of 455 mg/kg was known, a preliminary test to decide the highest level at 50, 100, 200 mg/kg/day for 7 day was conducted. At 200 mg/kg/day, decrease of body weight or suppression of body weight in both sexes, a change in the digestive tract e.g. the thickening of wall in

the forestomack and whitening in the duodenal were observed. At 100 mg/kg/day, similar changes were observed. Then the highest dose level for the test was set at 100 mg/kg/day.

Result : The NOAELs for repeat dose toxicity are considered to be 20 mg/kg/day for both sexes.

– Male:
At 100 mg/kg/day, no death was occured.
- By the observation, transient suppression of body weight gain and decrease in food consumption were observed.
- By the necroscopy findings, thickening of the wall of the forestomach and enlargement of the pancreatico-duodenal lymph nodes were observed.
- By the histopathological examination:
Ulceration, inflammatory cell infiltration and hyperplasia of the mucosa in the forestomach, and hyperplasia of plasma cells in the pancreatioco-duodenal lymph nodes were revealed.
- By the hematological and blood chemical examination:
A increase in reticulocyte, platelet and segmented neutrophil counts, a decrease in differential lymphocytes counts and albumin were revealed.
At 20 mg/kg/day, similar histopathological changes were observed in the forestomach.
At 4 mg/kg/day, no effects were observed.

Remark:
Thus the NOEL for males was considered as 4 mg/kg/day. However, Histopathological changes In forestomach were based on stimulative of 2-(dimethylamino)ethyl acrylate. Then the NOAEL for males was considered as 20 mg/kg/day.

– Female:
At 100 mg/kg/day, 2 females out of 12 died.
- By the observation, a decrease in the absolute thymus weight was observed.
- By the necroscopy examination, similar changes as males were observed.
- By the histopathological examination, similar changes as males were observed.
At 20 mg/kg/day and 4 mg/kg/day, no effects were observed.

The result of the hematological and blood chemical examination in male rats are summarized below.

Dose [mg/kg/day]	0	4	20	100
No. of animals	12	12	12	12
Reticulo (%)	25	27	26	30**
Plt [10E4/ul]	103	103	105	115*
Differential lymphocytes counts (%)	81	84	82	68**
Differential segmented neutrophils counts [10E2/ul]	16	12	15	39**
Albumin [g/dl]	3.7	3.8	3.7	3.6*

significantly different from control: * = p < 0.05, ** = p < 0.01

The major histopathological findings in rats are summarized below.

Male:

Dose [mg/kg/day]	Note	0	4	20	100
No. of animals		12	12	12	12

Findings in Lymph node (pancreatico-duodenal)					
-Hyperplasia, plasma cell	+	#	#	#	7/7
Finding in forestomach					
-Hyperplasia, mucosa	+	0	0	2	12**
-Inflammatory cell infiltration	+	0	0	1	0
	++	0	0	1	11**
-Ulcer	+	0	0	0	0
	++	0	0	1	11**

Note: + slight
++ moderate
# not examined

Female:

Dose [mg/kg/day]	Note	0	4	20	100	100
		(dead)				
No. of animals		12	12	12	10	2
Findings in Lymph node (pancreatico-duodenal)						
-Hyperplasia, plasma cell	+	#	#	#	7/7	#
Finding in forestomach						
-Hyperplasia, mucosa	++	0	0	0	10**	1
-Inflammatory cell inifiltration	++	0	0	0	10**	1
-Ulcer	++	0	0	0	9**	1

Source : MHW Japan (a)

Test condition : TEST ORGANISMS
- Age: 9 week old
– Weight at study initiation: male; 324 - 368 g, female; 212 - 244 g
– Number of animals: male; 12, female; 12
ADMINISTRATION / EXPOSURE
- Type of exposure: Oral feed by tube to stomach
- Vehicle: Corn oil, 5 ml/kg/day
– Concentration in vehicle: 0, 0.8, 4.0, 20 mg/ml
- Doses: 0, 4, 20, 100 mg/kg/day
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: daily
– Mortality: daily
- Body weight and Food consumption:
males and females; 0, 3, 7, 14 day from dose start, after then, one day per week. At mated female, 0, 7, 14, 20 day from pregnancy and 0, 4 day from lactation.

Conclusion : The NOAEL is considered to be 20 mg/kg/day for both sexes.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

20.02.2003 (45)

Type : OECD TG 408

Species : rat

Sex : male/female

Strain : Sprague-Dawley

Route of admin. : gavage

Exposure period : 13 week

Frequency of treatment : once daily

Post obs. period : 4 week

Doses : 2, 10, and 50 mg/kg/day

Control group : yes, peanuts oil

NOAEL : = 10 mg/kg bw

Method : OECD Guide-line 408 “Subchronic Oral Toxicity – Rodent: 90 day Study“

Year : 1997
GLP : yes
Test substance : Other TS: 99.9 % purity, Atofina SA Paris la Défense, Lot No. 004925
Result : TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:

- Mortality and time to death: A total of 22 (13 male and 9 female) animals died or were killed on humane grounds. All but one (a male) of these deaths occured during the treatment period. Signs of ill health and respiratory difficulty were observed prior to death in the mortality of animals. The cause of death, where evident, was lung lesions, which were considered to be due to direct irritation from regurgitated stomach contents.
- Clinical signs: No clinical signs related to treatment were observed in the males and females in the content group or those given 2 and 10 mg/kg/day.
  At 50 mg/kg/day, commencing from week 2-3, ptyalism, generally lasting to week 6/7, was observed in the majority of the animals which survived the treatment or treatment and recovery periods. In a few animals, this was accompanied by a short period(s) of loud breathing and/or less frequently signs of ill health. Ptyalism and loud breathing, in one male animal, were the only clinical signs observed in the recovery period.
- Body weight gain:
  Body weight and body weight gain in male animals given 2 or 10 mg/kg/day were unaffectedby treatment. In females given 2 or 10 mg/kg/day and males and females given 50 mg/kg/day there was dose related, transient reduction in body weight gain (which was only occasionally statisticcaly significant) from weeks 1/2 lasting up to 1- 4 week. Thereafter body weight gain improved and overall body weight gain for the treatment and recovery periods was considered to be unaffected by treatment.

– Food consumption:
Food conmsumption and effiency of food utilisation were unaffected by treatment and values, where calculable, were similar in all groups, including controls throughout the treatment and recovery periods.

- Ophthalmoscopic examination:
  There were no ophthalmic lesions, which could be related to treatment or previous treatment, detected during the examinations performed at the end of the treatment and recovery periods.

– Haematology:
There were no effects of treatment on any of the parameters examined in male or female animals given 2 and 10 mg/kg/day for 13 week.
At 50 mg/kg/day, there was a statitically significant increase in neutrophil counts (males and females), and an associated decrease in lymphocyte counts (males only; not significant) in animals given this substance for 13 week.
Total white cell counts were unaffected and the effect was not present, values being similar to controls, at the end of the recovery period.

- Blood biochemistry and urinalysis:
  There were no effects which could definitely be related to treatment with 2-(dimethylamino)ethyl acrylate at 2, 10 or 50 mg/kg/day for 13 week or 13 week followed by a four-week recovery period.
- Organ weights:
  There were no changes in absolute or relative organ weights which were considered to be related to treatment with 2,10, or 50 mg/kg/day of this substance or of toxicological significance after 13 week or 13 week followed by a four-week recovery period.
- Gross pathology:
  There were no effects of treatment on any of the tissues examined in male or female animals given 2 or 10 mg/kg/day for 13 week.

At 50 mg/kg/day the following changes, considered to be related to treatment period:
- greyish foci in the mucosa of the forestomach in 11/20 males and 3/19 females,
- enlaragement of the pancreatic lymph nodes in 5/20 males and 6/19 females,
- dilatation and/or reddish colour of the lungs in 7/20 males and 6/19 females.

None of the above findings were seen in animals killed at the end of recovery period.

– Histopathology:
At 10 mg/kg/day, hyperplasia/hyperkeratosis and edema and inflammatory cell infiltration (all due to direct irritance of this substance) of the forestomach submucosa were seen in (mostly) some males.
At 50 mg/kg/day, the following findings, considered to be treatment related, were seen in decedents and surviving animals after 13 week treatment.
- ulceration, hyperplasia/hyperkeratosis, inflammatory cell infiltration and/or granulation tissue formation in the submucosa, edema in the mucosa and submucosa and necrosis of the mucosa/submucosa in the forestomach.

These findings were considered to be a direct irritant effect of 2-(dimethylamino)ethyl acrylate on the mucosa of the forestomach.

[male]: forestomach

group [mg/kg/day]	0	2	10	50
no. of animals	10	not tested	0	20
edema in mucosa				
grade 1	0		0	4
grade 2	0		0	2
edema in submucosa				
grade 1	0		2	0
grade 2	0		1	3
grade 3	0		0	2
grade 4	0		0	1
granulation tissue formation in submucosa				
grade 1	0		0	2
grade 2	0		0	3
grade 3	0		0	1
inflammatory cell infiltration				
grade 1	0		1	2
grade 2	0		0	5
grade 3	0		0	2
ulceration				
grade 1	0		0	2
grade 2	0		0	4
grade 3	0		0	1
hyperplasia				
grade 1	0		2	2
grade 2	0		0	4
grade 3	0		0	6
hyperkeratosis				
grade 1	0		2	3
grade 2	0		0	4
grade 3	0		0	5

grade 1 = minimal, grade 2 = slight, grade 3 = moderate, grade 4 = marked

[female]: forestomach

group [mg/kg/day]	0	2	10	50
no. of animals	10	not tested	0	20
edema in mucosa				
grade 1	0		0	4
grade 2	0		0	2
edema in submucosa				
grade 1	0		0	3
grade 2	1		1	3
grade 3	0		0	3
grade 4	0		0	0
granulation tissue formation in submucosa				
grade 1	0		0	2
grade 2	0		0	6
grade 3	0		0	0
inflammatory cell infiltration				
grade 1	0		0	5
grade 2	0		0	5
grade 3	0		0	1
ulceration				
grade 1	0		0	1
grade 2	0		0	1
grade 3	0		0	1
hyperplasia				
grade 1	0		1	0
grade 2	0		0	2
grade 3	0		0	11
hyperkeratosis				
grade 1	0		1	0
grade 2	0		0	3
grade 3	0		0	10

grade 1 = minimal, grade 2 = slight, grade 3 = moderate, grade 4 = marked

- alveolar haemorrhage and/or oedema and congestion in the lungs which were considered likely to be an effect of regurgitation of stomach contennts.

Source : Atofina SA Paris la Défense

Test condition : TEST ORGANISMS
- Age: 6 - 7 week
- Weight at study initiation: mean dody weight 218 (male) and 180 (female)
- Number of animals:

group [mg/kg/day]	male	female
control	20	20
2	10	10
10	10	10
50	25	25

ADMINISTRATION / EXPOSURE
- Post exposure period: 4 weeks
- Vehicle: peanut oil
- Concentration in vehicle: 0, 0.667, 3.333, 16.67 mg/ml
- Total volume applied: 3 ml/kg/day

CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: at least once a day
- Mortality: at least twice a day (treatment period), or once a day (recovery period)

- Body weight: once before allocation of the animals into groups, on the first day of treatment and then once a week untill the end of the study.
- Food consumption: once a week
- Ophthalmoscopic examination: once before the beginning of the treatment period and on one occasion in weeks 13 and 17 (recovery period)

Result : 2-(dimethylamino)ethyl acrylate was administered daily by oral gavage to four groups of Sprague-Dawley rats at dose-levels of 0, 2, 10 and 50 mg/kg/day for 13 weeks, followed by a four-week treatment free period. This sustance was clinically well tolerated at 2 and 10 mg/kg/day at the latter dose-level, treatment-related lesions (which were not associated with any adverse clinical signs) were found in the forestomach of (mostly) some males.
At 50 mg/kg/day, a high incidence (13 males and 9 females) of mortality was observed. Before death, respiratory difficulties and sign of ill health were observed. In surviving animals of this dose-level, ptyalism and periods of loud breathing were the main signs noted, together with increased neutrophil counts at the end of the treatment period.
At histopathological investigations, this substance related lesions in the lungs and forestomach were found for both decedent animals and survivors.
Under the experimental conditions in the laboratory, the NOAEL of 2-(dimethylamino)ethyl acrylate, when administered daily, by oral gavage, to Sprague-Dawley rats for 13 weeks is therefore considered to be 10 mg/kg/day.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.02.2003 (16)

Conclusion : Repeated dose 90-day oral toxicity study in rodents [OECD TG 408] was conducted with SD (Crl: CD) rats at 0, 2, 10 and 50 mg/kg/day administered by gavage. At 50 mg/kg/day, the macroscopic lesions were limited to sporadic lung damage that is caused by reflux of stomach content. Judging from the hyperplasia/keratosis or other irritation changes found in forestomach, the reflux is a result of incontinence in gastro-intestinal tract. This substance was not toxic at 2 and 10 mg/kg/day. At the latter dose-level, treatment-related lesions were found in the forestomach of 4 males, however, these findings were almost of minimal grade which were not regarded to be adverse effect. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422] was also available with SD (Crj: CD) rats at doses of 0, 4, 20 and 100 mg/kg/day administered by gavage. The toxicity revealed is common in the two studies. At 100 mg/kg/day, the similar changes at 50 mg/kg/day in the former study was observed. At 20 mg/kg/day, the similar changes in the forestomach were observed in 2 males. However, these changes were not statistically significant, and considered not toxicologic by the authors. This substance was not toxic at 20 mg/kg/day in both sexes in the combined study. Nevertheless, the NOAEL was considered to be 10 mg/kg/day in the 90-day study, by the author.

Source : SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]
28.05.2003

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella Typhimurium TA 98, TA100, TA1535, TA1537
Concentration : 0, 10, 33, 100, 333, 1000, 3333, 10000 ug/plate
Cycotoxic conc. :
Metabolic activation : with and without

Result : negative
Method : other: no data
Year : 1987
GLP : no data
Test substance : As prescribed by 1.1 - 1.4
Remark : S9 mix used for metabolic activation was hamster and rat originated.
Result : 2-(dimethylamino)ethyl acrylate was negative in any of S. typhimurium TA98, TA100, TA1535 and TA1537 at the doses of 10 to 10,000 ug/plate with hamster S9, with rat S9, and without S9. Toxic effects were observed at 3333 ug/plate (TA98, TA100), 1000 ug/plate (TA1535, TA1537) with and without each S9.
Conclusion : negative
Source : NIPPON SHOKUBAI CO.,LTD. Osaka
Test condition : SYSTEM OF TESTING
- metabolic activation system: 10% S-9 mix from male Sprague-Dawley and male Syrian hamster livers, induced with Aroclor 1254.

ADMINISTRATION:
- plates per test: 3
- application: pre-incubation at 37° C, without shakinng, for 20 min.
- sovent: DMSO

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
20.01.2003 (61)

Type : Ames test
System of testing : Salmonella typhimurim TA100, TA1535, TA98, TA1537, Escherichea coli WP2 uvrA
Concentration : -S9 mix: 156 - 5000 micro g/plate +S9 mix: 156 - 5000 ug/plate
Cycotoxic conc. : -S9 mix: more than 1500 ug/plate at TA98 and TA1537, more than 5000 ug/plate at other, +S9 mix: more than 5000 ug/plate at other of WP2 uvrA
Metabolic activation : with and without
Result : positive
Method : Guidelines for screening mutagenicity testing of chemicals, JAPAN and OECD Guide-line 471 "Genetic Toxicology: Salmonella typhimurim, Reverse Mutation Assay" and 472 "Genetic Toxicology: Escherichea coli, Reverse Mutation Assay"
Year : 1997
GLP : yes
Test substance : other TS: 99.9 wt% purity, NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Positive
- Without metabolic activation: Negative

FREQUENCY OF EFFECTS:

(1)Positive result on the activation method (+S9) at TA98

Substance	Concentration [ug/plate]	Number of colonies/plate ± mean S.D. 1st test	2nd test
ADAME	0	32±2.3	24±2.3
	156	26±5.0	29±8.7
	313	19±5.2	32±2.9
	625	19±2.6	18±6.0
	1250	21±3.8	23±3.5
	2500	26±2.5	28±1.0
	5000	41±5.9	55±10.5
positive control	0.5	319±6.4	324±29.6

ADAME = 2-(dimethylamino)ethyl acrylate
positive control = 2-Aminoanthracene

(2)Confirmation test

Substance	Concentration [ug/plate]	Number of colonies/plate ± meanS.D.
ADAME	0	29± 6.2
	1000	23± 3.5
	1800	36±11.0
	2600	56± 5.9
	3400	65±11.0
	4200	70±11.5
	5000	70± 6.5
Positive control	0.5	283±29.1

Source : MHW Japan (b)
Test condition : SYSTEM OF TESTING
- Metabolic activation system: S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone
- No. of metaphases analyzed:
ADMINISTRATION:
- Number of replicates: 2
- Plates per test: 3
- Application: pre-incubation
- Positive and negative control groups and treatment:
- Pre-incubation time: 48 hr
DESCRIPTION OF FOLLOW UP REPEAT STUDY: A confirmation test was conducted for TA 98 which showed positive result.
CRITERIA FOR EVALUATING RESULTS:
(1) The revertant colony on this substance increase should be more than two times of the control.
(2) The concentration dependency should be shown in the revertant colony increase.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
28.05.2003 (46)

Conclusion : 2-(dimethylamino)ethyl acrylate did not induce gene mutations in 3 strains of *Salmonella typhimurium* and in *Escherichia coli* but did induce gene mutations in the TA98 strain with metabolic activation in one out of two studies.
Source : SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]
28.05.2003

Type : Cytogenetic assay
System of testing : Human lymphocytes
Concentration : 2.5 – 40 ug/ml without metabolic activation, 9.8 – 156 ug/ml with metabolic activation
Cycotoxic conc. : without metabolic activation: 156 ug/ml, with metabolic activation: 313 ug/ml
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : The highest concentration analyzed in the presence of metabolic activation, 156 ug/ml, caused an increase in the level of metaphase figures containing chromosomal aberrations which was statistically significant ($p < 0.01$ including gap damage, $p < 0.05$ when gap damage was excluded). Although the propotion of damaged cells seen, 3.5%

excluding gap damage and 4.0% including gap damage, falls within the historical controle range of means observed in the laboratory (0 - 5.25% and 0 - 6.25% repectively)
the level of complex damage seen, was unusually high at 1% (complex damage includes interchanges, complex rearragements, rings, dicentric chromosomes, pulverised cells and cells containing more than ten aberrations). The historical control data for complex damage observed in the laboratory in 83097 metaphase figures analysed has a range of 0 – 0.75% with a mean of 0.03%. Due to the rare occurrence of complex damage in human lymphocytes, greater significance is attached to this than other damage such as breakes. The result, therefore, indicates that clastogenic activity has been seen.
In the repeat analysis in the presence of metabolic activitation.
130 ug/ml of 2-(dimethylamino)ethyl acrylate caused an increase in chromosomal damage which was significant ($p < 0.01$). The level of damage seen (3%) again falls within the historical control range of means, however some complex damage was seen (0.5%) which supports the conclusion of the first analysis.

Result : GENOTOXIC EFFECTS:

- (a) Without metabolic activation:

Substance	Concentration [ug/ml]	No. of aberrant cells Excluding gaps % Mean	Including gaps % Mean
Control solvent	0.0	0–5.25 0.5	0–6.5 0.5
ADAME	2.5	1.0	1.0
	15.0	1.5	2.0
	25.0	5.5***	7.0***
	30.0	6.5***	7.5***
Ethylmethane sulphonate	750	19.0***	19.5***

Type of aberrations

Substance	Concentration [mg/ml]	No. of cells analysed	No. of structual aberrations BWF	I	SM	A	GT	CHR
Solvent	0	400	1	0	2	0	0	0
ADAME	2.5	200	0	0	1	1	0	0
	15.0	200	1	0	1	1	0	1
	25.0	200	0	1	3	6	3	4
	30.0	200	0	0	4	18	0	4
Ethylmethane sulphonate	750	200	1	0	4	51	1	3

ADAME = 2-(dimethylamino)ethyl acrylate
BWF: chromatid break with fragment
I: interchange
SM: single minute
A: acentric fragment
GT: greater than 10 aberrations
CHR: chromatid gap

- (b) With metabolic activation:

Substance	Concentration	No. of aberrant cells

	[ug/ml]	Excluding gaps % Mean	Including gaps % Mean
Conrol		0–5.25	0–6.25
solvent	0.0	0.5	1.0
ADAME	19.5	1.0	1.0
	78.2	0.0	0.0
	156	3.5**	4.0**
Cyclophophamid	20	14.0***	14.0***

Type of aberrations

Substance	Concen-tration [mg/ml]	No. of cells analysed	No. of structual aberrations I	SM	A	GT	CHR		
Solvent	0	400	0	1	1	0	2		
ADAME	19.5	200	0	1	2	0	0		
	78.2	200	0	0	0	0	0		
	156.0	200	1	4	14	1	2		
Cyclophophamid	20.0	200	2	7	29	1	2		

ADAME = 2-(dimethylamino)ethyl acrylate
I: interchange
SM: single minute
A: acentric fragment
GT: greater than 10 aberrations
CHR: chromatid gap

- (b') repeat With metabolic activation:

Substance	Concentration [ug/ml]	Excluding gaps % Mean	Including gaps % Mean
solvent	0	0.0	0.25
ADAME	90	1.0	1.0
	110	0.5	0.5
	130	3.0**	3.5**
Cyclophophamid	20	17.7***	17.7***

Type of aberrations

Substance	Concen-tration [mg/ml]	No. of cells analysed	No. of structual aberrations BWF	SM	A	GT	CHR		
Solvent	0	400	0	0	0	0	1		
ADAME	90	200	1	1	0	0	0		
	110	200	0	0	2	0	0		
	130	200	1	2	4	1	2		
Cyclophophamid	20.0	186	1	8	46	3	4		

ADAME = 2-(dimethylamino)ethyl acrylate
BWF: chromatid break with fragment
SM: single minute
A: acentric fragment
GT: greater than 10 aberrations
CHR: chromatid gap

Statitical analysis used was Fisher's test
*** = p < 0.001
** = p < 0.01
* = p < 0.05
no mark = p > 0.05

PRECIPITATION CONCENTRATION: none
TEST-SPECIFIC CONFOUNDING FACTORS: 2-(dimethylamino)ethyl acrylate is readly hydrolyzed.

Source : Atofina SA Paris la Défense

Test condition : SYSTEM OF TESTING
- Species/cell type: Human lymphocytes
- Metabolic activation system: Mixed-function oxidase systems in the rat liver were stimulated a single i/p injection of Aroclor 1254 (diluted in Arachis oil to 200 mg/ml) at a dose of 500 mg/kg. On the fifith day after treatment, the rats were killed.
- No. of metaphases analyzed: aberrations;100

ADMINISTRATION:
- Dose: -S9; 2.5, 15.0, 25.0, 30.0 ug/ml
+S9; 19.5, 78.2, 156.0 ug/ml
+S9 (repeat); 90, 110, 130 ug/ml
- Number of replicates: 2
- Application: diluted with sterile distilled water
- Positive and negative control groups and treatment, aberration:
-S9; negative control; Sterile distilled water 10 ug/ml, 0.5%
positive control; Ethyl methane sulphonate 750 ug/ml, 19.0 - 19.5%
+S9; negative control; Sterile distilled water 10 ug/ml, 0.0 - 1.0%
positive control; Cyclophosphamide 20 ug/ml, 17.7%

CRITERIA FOR EVALUATING RESULTS: Fisher's test

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

20.02.2003 (12)

Type : Chromosomal aberration test

System of testing : Chinese hamster lung (CHL/IU) cells

Concentration : 24 and 48 hr Continuous treatment: 0.015 - 0.12 mg/ml
6 hr short-time treatment without S9 mix: 0.0050 - 0.080 mg/ml
6 hr short-time treatment with S9 mix: 0.025 - 0.40 mg/ml

Cycotoxic conc. : 24 hr continuous tratment: 0.06 mg/ml
6 hr short-term treatment without S9 mix: 0.04 mg/ml
6 hr short-term tratment with S9 mix: 0.20 mg/ml

Metabolic activation : with and without

Result : positive

Method : Guidelines for screening mutagenicity testing of chemicals, JAPAN and OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"

Year : 1997

GLP : yes

Test substance : other TS: 99.9 wt% purity, NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07

Result : GENOTOXIC EFFECTS:

Table 1: Chromosome analysis continuously treated without metabolic activation: Time of exposure; 24 hours

Substance	Concentration [mg/ml]	Total no. of aberration cells (%) Including gaps	Total no. of aberration cells (%) Excluding gaps	Polyploid %	Concurrent cytotoxicity
Control		1.5	1.5	0.50	-
Solvent	0	0.0	0.0	0.38	100.0
ADAME	0.015	1.0	1.0	0.50	82.5
	0.030	0.5	0.5	0.50	72.0
	0.060	23.5*	21.0	10.75*	65.0
	0.12**	-	-	-	13.0
Mitomycin C	0.00005	47.0	45.5	0.13	-

Type of aberrations

Substance	Concentration [mg/ml]	No. of cells analysed	No. of structual aberrations gap	ctb	cte	csb	cse	mul	total	Others
Control		200	0	2	2	0	0	0	4	0
Solvent	0	200	0	0	0	0	0	0	0	0
ADAME	0.015	200	0	0	0	2	1	0	3	0
	0.030	200	0	1	0	0	0	0	1	0
	0.060	200	8	23	44	1	1	0	77	0
	0.12**	-								
Mitomycin C	0.00005	200	6	32	109	1	0	0	148	0

ADAME = 2-(dimethylamino)ethyl acrylate
gap: chromatid gap and chromosome gap
ctb: chromatid break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations
Notes
* : Significantly different from historical solvent control data at $p < 0.05$ by Fisher's exact test using a Bonferroni correction for multiple comparisons.
**: Chromosomal analysis was not performed because of severe cytotoxicity.

Table 2: Chromosome analysis continuously treated without metabolic activation: Time of exposure; 48 hours

Substance	Concentration [mg/ml]	Total no. of aberration cells (%) Including gaps	Total no. of aberration cells (%) Excluding gaps	Polyploid %	Concurrent cytotoxicity
Solvent	0	0.0	0.0	0.63	100.0
ADAME	0.015	3.5	2.5	0.26	58.5
	0.030	4.4	3.3	0.36	56.5

	0.060	8.5	8.5	6.21*	103.5
	0.12**	-	-	-	8.0
Mitomycin C	0.00005	49.0	48.0	0.25	-

Type of aberrations

Substance	Concentration [mg/ml]	No. of cells analysed	No. of structual aberrations gap	ctb	cte	csb	cse	mul	total	Others
Solvent	0	200	0	0	0	0	0	0	0	1
ADAME	0.015	200	3	4	0	2	0	0	9	1
	0.030	200	3	3	0	9	1	0	16	1
	0.060	200	0	4	10	11	2	10	37	4
	0.12**	-								
Mitomycin C	0.00005	200	6	35	127	12	7	20	207	1

ADAME = 2-(dimethylamino)ethyl acrylate
gap: chromatid gap and chromosome gap
ctb: chromatid break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations

Notes

* : Significantly different from historical solvent control data at $p < 0.05$ by Fisher's exact test using a Bonferroni correction for multiple comparisons.

**: Chromosomal analysis was not performed because of severe cytotoxicity.

Table 3: Chrosome analysis treated without metabolic activation:
Time of exposure; 6 – 18 hours (treatment – recovery)

Substance	Concentration [mg/ml]	Total no. of aberration cells (%) Including gaps	Excluding gaps	%	Polyploid cytotoxicity	Concurrent
Control		0.0	0.0	1.00		-
Solvent	0	1.0	1.0	0.13		100.0
ADAME	0.0050	2.0	1.0	1.25*		97.5
	0.010	16.0*	15.0	10.88*		99.0
	0.020**	-	-	-		17.0
	0.040**	-	-	-		15.5
	0.080**	-	-	-		17.0
CPA	0.005	0.5	0.0	0.25		-

Type of aberrations

Substance	Concentration [mg/ml]	No. of cells analysed	No. of structual aberrations gap	ctb	cte	csb	cse	mul	total	Others
Control		200	0	0	0	0	0	0	0	0
Solvent	0	200	0	0	1	0	1	0	2	0
ADAME	0.0050	200	2	0	1	1	0	0	4	0
	0.010	200	4	12	39	1	0	0	56	0

		0.020**	-								
		0.040**	-								
		0.080**	-								
CPA	0.005	200	1	0	0	0	0	0	1	-	

ADAME = 2-(dimethylamino)ethyl acrylate, CPA: cyclophosphamide
gap: chromatid gap and chromosome gap
ctb: chromatid break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations
Notes
* : Significantly different from historical solvent control data at p < 0.05 by
Fisher's exact test using a Bonferroni correction for multiple comparisons.
**: Chromosomal analysis was not performed because of severe cytotoxicity.

Table 4: Chrosome analysis treated with metabolic activation:
Time of exposure; 6 – 18 hours (treatment – recovery)

Substance	Concentration [mg/ml]	Total no. of aberration cells (%) Including gaps	Excluding gaps	Polyploid %	Concurrent cytotoxicity
Solvent	0	1.5	1.5	0.00	100.0
ADAME	0.025	0.5	0.5	1.25*	85.0
	0.050	12.5*	9.5	5.25*	80.0
	0.10**	-	-	-	39.0
	0.20**	-	-	-	36.0
	0.40**	-	-	-	37.5
CPA	0.005	92.5	92.0	0.13	-

Type of aberrations

Substance	Concentration [mg/ml]	No. of cells analysed	No. of structual aberrations gap	ctb	cte	csb	cse	mul	total	Others
Solvent	0	200	0	2	0	5	0	0	7	2
ADAME	0.025	200	0	1	0	0	0	0	1	0
	0.050	200	6	7	15	0	0	0	28	0
	0.010**	-								
	0.020**	-								
	0.040**	-								
CPA	0.005	200	8	86	387	11	3	615	0	

ADAME = 2-(dimethylamino)ethyl acrylate, CPA: cyclophosphamide
gap: chromatid gap and chromosome gap
ctb: chromatid break
cte: chromatid exchange
csb: chromosome break
cse: chromosome exchange (dicentric and ring)
mul: multiple aberrations
Notes
* : Significantly different from historical solvent control data at p < 0.05 by

Fisher's exact test using a Bonferroni correction for multiple comparisons.
**: Chromosomal analysis was not performed because of severe cytotoxicity.

Source	:	MHW Japan (c)
Test condition	:	SYSTEM OF TESTING - Species/cell type: CHL/IU from JCRB on Feb.1988 - Metabolic activation system: S9; Rat liver, induced with phenobarbitol and 5,6-benzoflavone - No. of metaphases analyzed: structural aberrations; 200, Polyploid; 800 ADMINISTRATION: - Dose: 24 and 48 hr Continuous treatment; 0.015, 0.030, 0.060 mg/ml 6 hr short-term treatment without S9 mix; 0.0050, 0.010 mg/ml 6 hr short-term treatment with S9 mix; 0.025, 0.050 mg/ml – Number of replicates: 2 – Solvent: distilled water – Application: - Positive control groups and treatment: -S9 mix, Mitomycin C +S9 mix, Cyclophosphamide - Pre-incubation time: 3 day DESCRIPTION OF FOLLOW UP REPEAT STUDY: none CRITERIA FOR EVALUATING RESULTS: Fisher's exact analysis
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
20.02.2003		(47)
Conclusion	:	*In vitro*, 2-(dimethylamino)ethyl acrylate was only weakly positive in the highest dose tested in CHL lung cells and human lymphocytes with and without metabolic activation.
Source	:	SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]
28.05.2003		

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	Swiss OF1 / CO: OF1(IOPS Caw)
Route of admin.	:	i.p.
Exposure period	:	twice separated by 24 hr
Doses	:	75 mg/kg
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	1993
GLP	:	yes

Test substance : Other TS: 99.87% purity, E Atofina SA, Lot No. RN 108

Result : MORTALITY:
2 animals were found dead 48 hr after the 2nd injection,
2 of the supplementary animals replaced those which died.
CLINICAL SIGNS: Piloerection and hypokinesia were observed.
GENOTOXIC EFFECTS:
In all groups, treated with 2-(dimethylamino)ethyl acrylate, the mean value of micronucleated polychromatic erythrocytes were similar to those of their respective vehicle groups at each sampling time, and no statistical significant differences weres observed. Moreover, 24 hr after the 2nd administration, the PE/NE ratio decreased significantly ($p < 0.001$) from that of the respective vehicle control groups, showing the toxic effect of 2-(dimethylamino)ethyl acrylate to bone marrow cells. 48 hr after the 2nd administration, the ratio had decreased but not statistically significantly due to the fact that the ration of one female was high compared to the ration of the other animals, despite the poor number of PE scorable.

- Time of sacrifice: 24 hr after the 2nd administration:

Group	doses [mg/kg]	MPE/PE Mean (SD)	PE/NE ratio Mean (SD)
vehicle	-----	2.0 (0.8)	0.7 (0.2)
ADAME	75	1.5 (1.1)	0.3 (0.1)
CPA	25	18.2 (3.8)#	0.4 (0.1)#

ADAME = 2-(dimethylamino)ethyl acrylate

- Time of sacrifice: 48 hr after the 2nd administration:

Group	doses [mg/kg]	MPE/PE Mean (SD)	PE/NE ratio Mean (SD)
vehicle	-----	1.9 (0.8)	0.9 (0.4)
ADAME	75	1.3 (0.9)	0.5 (0.5)

10 animals (5 males, 5 females) per group #: $p < 0.001$
Vehicle: physiological solution CPA: cyclophosphamide
PE: polychromatic erythrocytes NE: normochromatic erythrocytes
MPE/PE: micronucleated polychromatic erythrocytes/1000 polychromatic erythrocytes. (SD): standard deviation.

Source : Atofina SA Paris la Défense

Test condition : TEST ORGANISMS:
- Age: 6 week
- Weight at study initiation: 30 - 36 g for the males,
24 - 29 g for the females
- No. of animals per dose: 2 groups, each comprising 5 males and 5 females and one additional group conposed of 3 males and 3 females.

ADMINISTRATION:
- Vehicle: 10 ml/kg, physiological solution of 0.9% NaCl
- Duration of test: 48hr
- Frequency of treatment: twice separeted 24 hr
- Sampling times and number of samples: all animals 24 hr and 48 hr after the 2nd administration.
- Control groups and treatment:
Control; vehicle physiological solution of 0.9% NaCl and Cyclophosphamide at 2.5 mg/ml in distilled water.
Treatment; 75 mg/kg in physiological solution of 0.9% NaCl at a dose volume of 10 ml/kg

EXAMINATIONS:

- Analysis: For each animal, the micronuclei were counted in 2000 polychromatic erythrocytes; the polychromatic (PE) / normochromatic (NE) erythrocyte ratio was established by scoring a total of 1000 erythrocytes (PE+NE)
At each sampling time, the mean number of micronucleated olychromatic erythrocytes (MPE) and the PE/NE ration given for each animal of the treatred groups, are compared to the simultaneous vehicle groups.
- Criteria for evaluating results:
The results were considered negative if:
- A statistical significant increase in the number of MPE for at least one of the sampling time is recorded when compared to the vehicle groups.
–Tthis increased should double the number of MPE of the laboratory historical data.
- Criteria for selection of M.T.D.:
In the preliminary toxicity test, the i.p. administration of 100 mg/kg induced death of 3/6 animals within the 48 hr following the 2nd administration .
The i.p administration of 50 mg/kg induced only piloerection and emaciation, no mortality occured.
Consequently, 75 mg/kg a dose between 50 mg/kg (0% mortality) and 100 mg/kg (50% mortality) was defined as the Maximum Tolerated Dose.

Result : 2-(dimethylamino)ethyl acrylate did not induce cytogenetic damage to the bone marrow cells of mice when treated twice separated by 24 hr by intraperitoneal route at 75 mg/kg in the micronucleus test.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

20.02.2003 (14)

Conclusion : *In vivo,* 2-(dimethylamino)ethyl acrylate was negative when administered i.p. at the MTD in a single dose study. Based on the present results, and taking into account data on structurally related substances, it is unlikely that this substance is mutagenic *in vivo*.

Source : SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]

28.05.2003

5.7 CARCINOGENITY

MEMO : There is no carcinogenicity data. Based on mutagenicity data, this substance would not be expected to be carcinogenic.

Flag : Critical study for SIDS endpoint

28.05.2003

5.8 TOXICITY TO REPRODUCTION

Type : OECD combined study TG 422, combined repeat dose and reproductive/developmental (one generation) toxicity screening test

Species : rat

Sex : male/female

Strain : Sprague-Dawley

Route of admin. : gavage

Exposure period : males, 43 day
females, from 14 day before mating to day 3 of lactation

Frequency of treatment : once daily

Premating exposure period

Male : 14 day
Female : 14 day
Duration of test : males; 43 day, females; from 14 day before mating to day 4 of lactation - 54 day
Doses : 0(Vehicle), 4, 20, 100 mg/kg/day
Control group : yes, concurrent vehicle
Method : OECD combined repeated dose and reproductive/developmental toxicity screening test
Year : 1997
GLP : yes
Test substance : other TS: Purity 99.9%, NIPPON SHOKUBAI CO.,LTD., Lot No. 5P07
Remark : As the LD50 value of 455 mg/kg was known, a preliminary test to decide the highest level at 50, 100, 200 mg/kg/day for 7 day was conducted. At 200 mg/kg/day, decrease of body weight or suppression of body weight in both sexes, a change in the digestive tract e.g. the thickening of wall in the forestomack and whitening in the duodenal were observed. At 100 mg/kg/day, similar changes were observed. Then the highest dose level for the test was set at 100 mg/kg/day.
Result : For reproduction toxicity
NOAELs: = 100 mg/kg/day for males
= 100 mg/kg/day for females
= 100 mg/kg/day for F1 offsprings
2-(dimethylamino)ethyl acrylate had no effects on reproductive parameters such as the mating index, the fertility index, number of corpora lutea or implantations, the implantation index, the gestation index, the delivery index, gestation length, parturition or maternal behavior. On examination of neonates, these were no significant differences in number of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. No abnormal findings ascribable to the compound were found for external features, clinical signs or necroscopy of the offspring.

– Female:
At 100 mg/kg/day, 2 females out of 12 died.
- By the observation, a decrease in the absolute thymus weight was observed.
- By the necroscopy examination, similar changes as males were observed.
- By the histopathological examination, similar changes as males were observed.
At 20 mg/kg/day and 4 mg/kg/day, no effects were observed.
Female:

Dose [mg/kg/day]	Note	0	4	20	100	100
		(dead)				
No. of animals		12	12	12	10	2
Findings in Lymph node (pancreatico-duodenal)						
-Hyperplasia, plasma cell	+	#	#	#	7/7	#
Finding in forestomach						
-Hyperplasia, mucosa	++	0	0	0	10**	1
-Inflammatory cell inifiltration	++	0	0	0	10**	1
-Ulcer	++	0	0	0	9**	1

Reproductive parameters:

- Dose [mg/kg/day]	0	4	20	100
-Number of pairs examined	12	12	12	11#
-Number of pairs with successful mating	12	12	12	10

-Mating index (%)	100	100	100	100
-Number of pregnant females	11	11	11	9
-Fertility index (%)	91.7	91.7	91.7	90.0
-Pairing days until mating	2.0	2.1	2.0	3.6
-Number of estrous stages without mating	0	0	0	0

Mating index (%) = (No. of pairs with successful mating / No. of pairs examined) x 100
Fertility index (%) = (No. of pregnant animals / No. of pairs with successful mating) x 100

Developmental parameters:

- Dose [mg/kg/day]		0	4	20	100
-Number of females examined		11	11	11	8
-Live birth index (%)	98.6	99.4	98.7	95.1	
-Number of pups delivered		16.2	15.4	13.8	15.8
-Number of live pups on day 0		15.9	15.3	13.6	14.9
- Sex ratio (male/female)	0.97	0.91	1.14	0.89	
-Viability index on day 4 (%)		90.9	99.4	98.8	87.5
-Number of live pups on day 4		14.4	15.2	13.5	13.4
-Body weight gain of pups [g]					
day 0 to 4 male		4.3	4.3	4.2	3.8
female		4.2	4.3	4.2	3.7

Live birth index (%) = (No. of live pups on day 0 / No. of pups delivered) x 100
Viabitity index (%) = (No. of live pups on day 4 / No. of pups on day 0) x 100

Source : MHW Japan (a)
Test condition : ADMINISTRATION / EXPOSURE
- Type of exposure: Oral feed by tube to stomach
- Vehicle: Corn oil, 5 ml/kg/day
- Concentration in vehicle: 0, 0.8, 4.0, 20 mg/ml
- Doses: 0, 4, 20, 100 mg/kg/day

PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: daily

Test substance : SOURCE: NIPPON SHOKUBAI CO.,LTD. Lot No. 5P07
PURITY: 99.9 wt%
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.02.2003 (45)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Type : OECD TG 414
Species : rat
Sex : female
Strain : Crl: CD(SD) BR
Route of admin. : gavage
Exposure period : from day 6 to day 15 of pregnancy
The day of positive mating (assessed by observation of vaginal plug) was designated as day 0 post-coitum (p.c.).
Frequency of treatment : once daily
Duration of test : 20th day after mating
Doses : 10, 30 and 100 mg/kg/day
Control group : yes, peanuts oil

NOAEL Maternalt. : = 10 mg/kg bw
NOAEL Teratogen : = 30 mg/kg bw
Method : OECD Guide-line 414, “Teratogenicity“
Year : 1997
GLP : yes
Test substance : Other TS: 99.91% purity, Atofina SA, Lot No. RN 107
Result : The NOAELs for teratogenecityt are considered to be 30 mg/kg/day.

MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality and day of death: There were no deaths at 10 mg/kg/day. In each of the 30 and 100 mg/kg/day groups, 2/25 females were found dead and 1/25 females were killed urgently. Although no specific factors contributing to death were established, respiratory difficulties were observed in some animals and may have contributed to the deaths.

The pregnancy status of the females

group [mg/kg/day]	0	10	30	100
mated females in study	25	25	25	25
non-pregnant females	1	1	3	0
pregnant females	24	24	22	25
- died	0	0	2	2
- sacrificed prematurely	0	0	1	1
- total resportion	1	0	0	1
- pregnant, alive at term	24	24	19	22
- complete pregnancy	23	24	19	21

- Number pregnant per dose level:
- Number aborting: No abortions occered in any animal from any group.
- Number of resorptions: There were no tatal resorption at 10 and 30 mg/kg/day. One female given 100 mg/kg/day presented total resorption.
- Number of implantations:
- Pre and post implantation loss:
- Number of corpora lutea:
- Duration of Pregnancy:
- Food/water consumption and Body weight: The food comsumption and body weight gain of the females given 10 and 30 mg/kg/day were similar to those of the controls. The food comsumption and body weight bain of the females given 100 mg/kg/day were lower than those of the controls.

Mean food consumption of the females

group [mg/kg/day]	0	10	30	100
day 2 to 6	27	27	26	28
day 6 to 9	25	26	24	19##
day 9 to 12	26	27	24	22#
day 12 to 16	27	28	25	19##
day 16 to 20	31	31	30	26

Statistical : ANOVA + Dunnett-test, # = p<0.01, ## = p<0.001

Mean body weight of the females

group [mg/kg/day]	0	10	30	100
day 2	248	248	247	248
day 6	272	271	268	270

day 7	277	276	273	267#
day 8	281	281	277	266##
day 9	284	286	280	268###
day 10	293	294	287	276###
day 12	309	310	303	286####
day 14	322	324	314	296###
day 16	340	343	331	296###
day 20	401	407	398	363##

Statistical : ANOVA + Dunnett-test, # = p<0.05, ## = p<0.01, ### = p<0.001
- Description, severity, time of onset and duration of clinical signs: No treatment-related clinical signs were observed at 10 mg/kg/day. In the 30 and 100 mg/kg/day groups, 8/25 and 17/25 females presented signs of poor clinical condition, respectively (principally loud breathing, piloerection, chromorhinorrhea, round back, and dyspnea).
- Hematological findings incidence and severity:
- Clinical biochemistry findings incidence and severity:
- Gross pathology incidence and severity: No treatment-related macroscopic findings were observed at 10 mg/kg/day. In the 30 and 100 mg/kg/day groups, 3/25 and 6/25 females, respectively presented macroscopic findings involving the gastrointestinal tract (gaseous dilatation or thickening of mucosa). These findings were principally observed in the decedent animals.
- Organ weight changes:
- Histopathology incidence and severity:

FETAL DATA:
- Litter data: In the 10 and 30 mg/kg/day groups, the post-implantation loss was similar to the controls and no teatment-related effects were observed on the number of fetuses, the fetal body weight or the sex-ratio.
In the 100 mg/kg/day group, the post- implantation loss (represented by early and late resorptions) was increased and the body weight of the fetuses was decreased (this was considered to be, at least in part, an indirect consequence of the effect on the maternal body weight). The number of live fetuses and the sex-ratio were not affected at this dose-level.
- Postnatal growth:
- Postnatal survival:
- Grossly visible abnormalities:
- In external abnormalities: No external anomalies were noted in the 10 and 30 mg/kg/day groups. In the 100 mg/kg/day group, a total of 27/299 fetures suffered anomalies : 14 fetuses from the same litter were dwarf and 13 other futuses, from another litter, had adactyly.
- In internal examination: In the 100 mg/kg/day group, 2/144 fetuses had anomalies (one fetus had a cleft palate, other fetuses presented hydrocephaly, and six dwarf fetuses suffered testicular ectopia). The absence of ossification of many bones (vertebrae, sternebrae) were found.
- Fetal variations: reduced ossification of many bones (skull, vertebrae, sternebrae, limbs) were found and the incidence for the reduced of Ossification of 6th sternebra was increased at 100 mg/kg/day. At 30 mg/kg/day, reduced ossification of head and vertebrae were found.

Source : Atofina SA Paris la Défense

Test condition : TEST ORGANISMS
ADMINISTRATION / EXPOSURE
- Type of exposure: Oral gavage
- Duration of exposure: the period of organogenesis (day 6 to 15 post-coitus, inclusive)

- Treatment: A preliminary test was performed at 10, 30 and 100 mg/kg/day. No clinical signs were recorded at any dose-level. At 100 mg/kg/day, one mortality was recorded, and food consumption and body
weight gain were reduced over the first three days of treatment. No embryo or fetoxicity, nor signs of teratogenic effects were observed at any dose-level. On the basis of there findings, the same dose-levels were selected for use in the principal assay.
- Vehicle: peanut oil
- Concentration in vehicle: 0, 3.333, 10.00, 33.33 mg/ml
- Total volume applied: 3 ml/kg/day
- Doses: 0, 10, 30, 100 mg/kg/day

MATING PROCEDURES: Females were mated at the breeder'sfacilities. The day of positive mating (assessed by observation of vaginal plug) was designated as day 0 post-coitus.

PARAMETERS ASSESSED DURING STUDY:
- Body weight gain: on day 2, 6, 7, 8, 9, 10, 12, 14, 16 and 20 post-coitus
- Food consumption: at the intervals; day 2 - 6, 6 - 9, 9 - 12, 12 - 16 and 16 - 20 post-coitus
- Clinical observations: once a day
– Examination of uterine content: number of corpora lutea, number and distribution of dead and live fetuses, number and distribution of early and late resorption, number of implantation sites.
– Examination of fetuses: body weight, external examination, soft tissue examination, skeletal examination, sexes of fetuses

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC): the principal thoracic and abdominal organs

STATISTICAL METHODS: Mean values were compared by one-way analysis of variance and Dunnett's test. Percentage values were compared by Fischer's exact probability test.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
20.02.2003 (15)

Conclusion : A teratogenicity study [OECD TG 414] (0, 10, 30, 100 mg/kg/day) were conducted with SD (Crl: CD) rats. At 100 mg/kg/day, 27/299 fetuses showed anomalies (dwarf, adactyly) in external examination and 2/144 fetuses showed anomalies (cleft palate, hydrocephaly, testicular ectopia) in internal examination. The absence of ossification of various bones (vertebrae, sternebrae) were found in many individuals. Maternal toxicity including death was evident. At 30mg/kg/day, no teratogenic effects were observed, two females, however, died and this substance was found maternally toxic. Fetuses with reduced ossification were found at this dose. At 10 mg/kg, no adverse effect was evident. In the teratology study, the NOAEL for maternal toxicity in rats was 10 mg/kg. Prenatal developmental toxicity was only observed at doses (100 mg/kg) which produced signs of maternal toxicity and mortality. The NOAEL for reproduction/developmental toxicity and teratogenicity are considered to be 10 and 30 mg/kg/day respectively.

Source : SIDS INITIAL ASSESSMENT PROFILE [CAS NO 2439-35-2]
28.05.2003

5.10 OTHER RELEVANT INFORMATION

Remark : Results :
2-(dimethylamino)ethyl acrylate is a reversible, uncompetitive inhibitor of

choline acetyltransferase both *in vitro* and *in vivo* (Rowell and Chiou, 1976a-d).

Source : Atofina SA Paris la Défense
09.05.1994 (53)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Memo : VAPOR TOXICITY(1)
Remark : This substance was used in several of the screen printing ink formulations at one company in U.S.A, which occured severe eye irritation. Several cases of eye discomfort were serious enough to require emergency medical treatment and several-day convalescence periods for exposed workers. Duration of exposure in these cases was 6 hr or less. Removal of this substance from the formulations has eliminated the incidence of eye irritation.
Source : RHONE-POULENC INC
10.12.2002 (60)

Memo : VAPOR TOXICITY(2)
Remark : A company bought red and green UV ink for a large EAST Coast retailer's job. On October 2, in 1989, the workers began running the screen printing job. Two of senior printers incurred severe eye irritation (even with eye goggles on).
They returned the next day complaining of eye irritation, impaired vision, and problems with eating/ tasting of food. After a short while both left for the nearby Alliance Eye and Ear Clinic for checkup/treatment.
There the doctor indicated significant damage to the eyes had been done (the proctective cover of the retinus was "burned off"; with uncertainty of regrowth!).
Source : RHONE-POULENC INC
10.12.2002 (60)

Remark : In der Zeit vom 1.Januar 1989 bis September 1994 musste lediglich 1 Mitarbeiter, dem Produkt in das Gesicht gespritzt war, wegen einer Augenveraetzung in die Augenklinik zur stationaeren Therapie eingeliefert werden.
Source : Atofina SA Paris la Défense
30.09.1994 (25)

Remark : Report on one case of eye irritation after accidental exposure to DMEA, which was sent to the clinic for further treatment.
Source : BASF AG Ludwigshafen

Reliability : (2) valid with restrictions
basic data given, acceptable restrictions
04.06.1997 (24)

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